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RESPONSE OF CHRONIC SIMPLE GLAUCOMA TO TREATMENT WITH CYCLODIATHERMY PUNCTURE

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Two types of diathermic treatment have been recommended for glaucoma. In both types the diathermic current is applied to the ciliary region, thus influencing in one way or another that area of the bulbus which is supposed to play an important part in the mechanism for regulating the intraocular pressure. Weve,[1] followed by Amsler,[2] was first to use the surface electrode, a method later emphasized by C. H. Albaugh and Edwin B. Dunphy.[3] The perforating type, called cyclodiathermy puncture, was introduced by A. Vogt[4] and developed by him and his associate H. Wagner.[5] I had the privilege of attending the meeting at which Vogt made his rather sensational communication. I was at once strongly impressed by the revolutionary idea as well as by the promising results in the most desperate cases of glaucoma. I immediately began to use cyclodiathermy punctures and up to now I have had experience with well over a hundred cases.

Naturally, cyclodiathermy puncture was applied first only in desperate cases of glaucoma which had been unsuccessfully treated by several of the various surgical procedures. In the absence of extensive experience and of observations over a sufficient period of time, some theoretic objections called for conservative use of the method. Especially was the method excluded for chronic simple glaucoma in its uncomplicated form. Albaugh and Dunphy[3] made it clear that cyclodiathermy "is not a substitute for other glaucoma measures" and in the discussion of their paper Sanford R. Gifford emphasized the statement that this is "an operation not for simple glaucoma or for primary glaucoma."

However, as my own experience grew I became more and more convinced that the technic of cyclodiathermy puncture could be so refined as to practically exclude most of the dreaded unfavorable side and after effects. Whereas it is true that one sees many good results with the various operations now in use for glaucoma, there are also many failures. The more I saw of the course of glaucoma, especially in the Negro race, the more it became clear to me that the usual filtering operations, such as trephining, iridencleisis and cyclodialysis, could not be the definite answer to the problem. It must be acknowledged that Iliff[6] demonstrated that not all of the poor results of operations for glaucoma in the Negro are due to racial peculiarity; part are due to the advanced stage of glaucoma when the patients are first seen. Nevertheless I still believe, in agreement with most ophthalmologists who have had experience in treating Negroes for glaucoma, that the beneficial effect of a filtering operation is more likely to be nullified by cicatrization in the Negro than in white persons.

I therefore thought it was justifiable to treat with cyclodiathermy puncture a group of Negroes who were suffering from chronic simple glaucoma and who had not been previously subjected to any other operation. Should the treatment prove to be successful also in that type of glaucoma, and should no unfavorable reactions, side and after effects develop, no one would profit more from this experience than the Negro race.

This report will consist mainly of my experiences with such a group. To my knowledge it is the first time that cyclodiathermy puncture has been reported as being successfully used for uncomplicated chronic simple glaucoma.

It is not my purpose to discuss the theories concerning glaucoma in this paper, which is intended to deal with the problem in an essentially

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1. Weve, H., cited by Amsler.[2]

2. Amsler, M., in discussion on Vogt.[4a]

3. Dunphy, E. B., and Albaugh, C. H.: Cyclodiathermy: An Operation for the Treatment of Glaucoma, Tr. Am. Ophth. Soc. **39**:193, 1941.

4. Vogt, A.: (*a*) Versuche zur intraokularen Druckherabsetzung mittelst Diathermieschädigung des Corpus ciliare (Zyklodiathermiestichelung), Schweiz. med. Wchnschr. **67**:367, 1937; (*b*) Cyclodiathermypuncture in Cases of Glaucoma, Brit. J. Ophth. **24**:288, 1940; (*c*) Die Zyklodiathermiepunktur gegen Glaukom, Klin. Monatsbl. f. Augenh. **103**:591, 1939.

5. Wagner, H.: Diathermiestichelung des Corpus ciliare bei Glaukom, Schweiz. med. Wchnschr. **69**:883, 1939.

6. Iliff, C. E.: Surgical Control of Glaucoma in the Negro, Am. J. Ophth. **27**: 731, 1944.

practical way. However, before discussing the mode of action of cyclodiathermy puncture a few words may be said about how the mechanism of stabilizing the intraocular tension may be disturbed in the glaucomatous eye. The increase in intraocular tension characteristic of glaucoma may be brought about either by a blockage of the outflow of the intraocular fluid or by an abnormally increased production of this fluid. In the first case the drainage system is unable to evacuate the aqueous adequately although the latter may be produced in normal quantities. In the latter case the aqueous produced in abnormally large amounts cannot escape through a normal drainage system which would be sufficient in the presence of normal quantities of fluid. Accordingly, the approach to the problem of influencing the balance of the intraocular pressure may be either in the direction of increasing the outflow or of decreasing the inflow of the intraocular fluid. Most of the surgical measures for the control of tension in glaucoma, and I shall consider the surgical treatment exclusively in this study, tend to increase the outflow.

Fig. 1.—Result of cyclodiathermy puncture when a Vogt needle was used. The illustration on the left shows the untreated side; that on the right, the treated side.

Among those procedures which possibly might in part result in an inhibition of the aqueous-producing action of the ciliary body may be mentioned Heine's [7] cyclodialysis, Verhoeff's [8] cyclectomy and Guerry's [9] diathermic obliteration of the posterior long ciliary arteries.

The definite answer to the question why diathermy puncture reduces the tension of the eye has not yet been found. Vogt's original idea was that he was to destroy the ciliary body with its processes directly with the coagulating diathermic current. However, when the punctures were applied near the limbus where they reached the corona ciliaris, there was too much reaction and even necrosis of the cornea occurred. It was found that when cyclodiathermy puncture was applied farther back, to the pars plana of the ciliary body, the same result, a lowering of the tension, was obtained. In a specimen from an eye which had been enucleated following severe intraocular hemorrhage, after cyclodiathermy puncture had kept the eye, affected with absolute glaucoma, quiet for more than two years, one may find part of the explanation. Although the punctures had not reached the corona ciliaris and the ciliary processes directly, they became completely atrophied in the area treated, as can be seen by comparison with the ciliary body of the untreated side of the same eye (fig. 1). It must be assumed that by destroying the blood vessels, which are supplied by the long posterior ciliary arteries and reach the corona ciliaris by passing through the pars plana, the circulation of the corona ciliaris becomes impaired to a point at which degeneration and atrophy results. This obviously should ultimately lead to a decrease in production of intraocular fluid. Directly after the application of cyclodiathermy puncture, however, a congestive inflammatory stage may be present which increases the circulation in the whole eye. This also may cause a softening of

7. Heine, I.: Die Zyklodialyse, eine neue Glaucomoperation, Deutsche med Wchnschr. **31**:824, 1905.

8. Verhoeff, F. H.: Cyclectomy: A New Operation for Glaucoma, Arch. Ophth. **53**:228, 1924.

9. Guerry, DuP., III: Angiodiathermy of the Long Posterior Ciliary Arteries and Its Use in the Treatment of Glaucoma, Am. J. Ophth. **27**:1376, 1944.

the eye but, on the contrary, in some instances, is followed by a temporary rise of tension. I shall come back to that part of the problem later while discussing the results.

As already mentioned, the present study deals with cases of chronic uncongestive glaucoma of various stages that had not undergone surgical treatment in Negro patients. Recently I began to treat with cyclodiathermy puncture also white patients affected with uncomplicated chronic glaucoma. The results seem not to differ from those obtained in Negroes, and I shall later make a more complete report comprising all my experiences.

The patients were treated at Duke Hospital, McPherson Hospital and Lincoln Hospital. The majority were operated on by myself, the rest by the resident house officers, following closely the technic outlined by me.

The group comprises 16 eyes. In each case visual acuity, fields and tension without and with miotics were recorded for some time before the operation. The indication for operation was established as usual, i. e. when the tension could not be kept within normal limits by miotics or when fields and central vision showed signs of deterioration. The number of cyclodiathermy punctures were recorded and a note about the immediate postoperative course made. The tension determined by palpation or taken with the tonometer during the first few postoperative days was carefully watched. Vision, tension and fields were examined at regular intervals and for the purpose of this report the findings when the patient was last seen were recorded. The time of observation varied from one to ten months after the operation.

EFFECTS OF CYCLODIATHERMY PUNCTURE

I was interested in finding answers to the following questions:

1. Does cyclodiathermy puncture reduce the tension in simple chronic glaucoma, and if there is a reduction, how long does it last?

2. What influence does the operation have on the whole course of the glaucomatous disease, including vision, field and optic atrophy?

3. Is cyclodiathermy puncture accompanied by complications which would make it appear to be unsuitable for general use as a primary operation in simple chronic glaucoma?

As to the first question one must distinguish between the tension found immediately or a few days after the operation and the tension when last seen. It has been found by previous observers that immediately after cyclodiathermy there is sometimes not a reduction but, on the contrary, a temporary rise in pressure. This, however, occurs more frequently after surface cyclodiathermy than after cyclodiathermy puncture. In our series, in no case has the tension after the operation been found higher than before. In 1 case it had been unimproved and in another case improved but still higher than normal. In 15 cases the tension was definitely lowered within the first few days after cyclodiathermy puncture. It should be noted that the patients who did not show a satisfactory reduction of tension immediately after the operation were not among those who when last seen had abnormal tension. It would therefore seem that an occasional rise of tension shortly after the operation should have no influence on the final outcome. The period from the operation to the time when last seen naturally varies greatly. Although in a number of cases a much longer time has elapsed since operation, the longest time of observation was ten months. Unfortunately some of the patients after they had done well for some time did not continue to present themselves for the regularly scheduled examinations. The tension when last seen was unimproved in no case, improved but still too high in 3 cases, and improved within normal limits in 14. Among those with tension unimproved is included 1 case in which after a second operation the tension was found to be within normal limits.

As to the influence of cyclodiathermy puncture on the glaucomatous process as a whole, including vision, fields and optic atrophy, I think that one should differentiate between the very advanced cases with considerable loss of vision, large field defects and pronounced cupping with atrophy of the optic nerve and the more favorable cases in which the destruction has not yet reached that stage. Arbitrarily I place in the first group patients with central vision of 20/200 or less and marked field defects, and in the second group all patients with vision better than that. In the first group of 8 patients with greatly advanced disease central vision had improved in 2, had become worse in 1 and remained the same in 5. The fields were improved in 2 and the same in 6 cases. In no case did the field show further deterioration. However, in this group there were patients with vision so poor that no fields could be recorded either before or after the operation. If I list these cases as showing no change, this statement does not have much significance. Statistically these cases would have to be eliminated. These patients were among the first ones treated when we cautiously began to try out cyclodiathermy puncture in cases in which there was not

much to lose. In the second group with visual acuity better than 20/200 the central vision had improved in 3, had become worse in 1 and remained the same in 4 cases. The field had improved in 1, became worse in 1 and remained the same in 6 cases.

In 10 cases with the longest period of observation, four, six and one-half, nine and one-half and ten months, the tension was within normal limits in 8, improved but too high in 1 and unimproved in 1 case. Vision was better in 2 cases, worse in 2 and the same as before cyclodiathermy puncture in 6. The fields were worse in 1 case and stationary in 9 cases. As the number of observations is much too small for statistical use, I refrain from giving the results in percentages.

The third question, about complications that might make cyclodiathermy puncture appear unsuitable as a primary operation in chronic simple glaucoma, may be answered favorably as far as our present experience goes. Here again I shall consider the immediate postoperative course separately from the late effects on the eye. A moderate injection, without inflammatory signs in the anterior chamber, was common. Some eyes, however, showed surprisingly little reaction. Moderate reactions with slight irritation of the iris were seen in 2 instances. One patient had fibrinous exudate in the lower part of the anterior chamber, which however disappeared within one week without further complications. Most probably a slight technical mistake produced this accident, as some of the punctures had been placed too far forward in the ciliary body. I shall come back to this observation when discussing the technic. In 2 cases cyclodiathermy puncture was followed by much dispersion of pigment, with numerous deposits of pigment granules on the posterior surface of the cornea. When the patient was seen again after one month these deposits had completely disappeared and the tension was 10 and 13 (Schiøtz) respectively. In no case of this series had a hemorrhage into the anterior chamber occurred. This was in contrast with the experience in cases of hemorrhagic glaucoma, in which hemorrhages are not infrequently observed after cyclodiathermy puncture.

While the immediate complications accompanying this operation are negligible, late disturbances were even more conspicuous by their absence. Of course, no case of sympathetic ophthalmia was observed. Although I admit that fears of sympathetic ophthalmia had some theoretic background, the entirely negative experience of all ophthalmologists using cyclodiathermy puncture should lead one to discard this possibility as a serious objection to the method. It might well be that as the number of operations performed increase sympathetic opthalmia will occur in rare instances. But certainly there is no evidence that this disastrous disease occurs more frequently after this than after any other operation.

No incidence of infection, either postoperative or so-called late infection, has been observed. Late infection, as for instance that seen after trephining, is not to be expected, as there is no permanent opening left in the bulbus.

The complication I personally dreaded most was cataract, and I watched the lens in these cases for months with some anxiety. Careful study with slit lamp and ophthalmoscope was carried out every time the patient was seen. I state positively that no opacities which could be attributed to cyclodiathermy puncture were ever observed. I could not even see senile opacities progress faster than expected after the operation. The fact that the vision in general was well preserved during the months of observation after cyclodiathermy puncture is in line with this statement. However, I believe that it is wise for any one who wishes to use cyclodiathermy puncture to follow certain principles of technic in order to be safe. I shall come back to this point.

Friedenwald in discussing Dunphy's [3] paper raised the question about accommodation, astigmatism and gonioscopic appearance of the angle of the chamber. The accommodation could not be determined accurately because of the advanced age of most of the patients. So far as astigmatism is concerned I made one peculiar observation. In 1 case a patient who required a correction of —.75△ cylinder, axis 180 before the operation saw definitely better with the same cylinder, axis 90 a few weeks after the operation. Gradually he came again to require a sphere, and when last seen he took the same lens and the same axis as before cyclodiathermy puncture. I record this observation; however, I am hesitant to interpret it as definitely connected with the operation.

Gonioscopic observations were not carried out routinely, but no specific influence on the angle of the chamber was observed when it was used. However, one had the impression that the chamber in some cases had become slightly deeper.

A peculiar change in the pupil occurred in some cases. It remained slightly larger than before the operation; sometimes it was not quite exactly round as before and reacted sluggishly to light. This may have some relation to the disturbed innervation or may be caused by slight diffuse posterior synechia following a mild postoperative irritation.

After considering in detail all observations made after cyclodiathermy puncture it may positively be said that no side or after effects could be observed which would make this operation appear to be unsuitable as a primary operation for chronic simple glaucoma.

TECHNIC

A careful choice of technic is essential for successful results from cyclodiathermy puncture and the avoidance of complications. The ultimate goal must be to cause the least harm to the eye while producing maximum action against the glaucoma; i. e., there must be a permanent stabilization of the intraocular tension within normal limits.

A very fine and short needle must be used. Vogt's needle, 0.5 mm. long and 0.18 mm. in diameter, or the shortest type of Kronfeld's needle may be satisfactory. More recently I have been using exclusively a needle that has been made according to my own suggestions. It is better insulated and may be recommended.[9a] Very little current should be used. Vogt used to recommend 60 milliamperes. However, I found that it was not practical to rely on a milliampere meter and that it was necessary to determine at the beginning of the operation how much current is necessary to just produce coagulation on the surface of the sclera. Usually the Walker machine is set between 15 and 20.

Fig. 2.—Result of cyclodiathermy puncture when Walker micropins were used. Arrow shows herniation of ciliary body into sclera.

The importance of a proper needle is made clear in comparing figures 1 and 2. In the first case a Vogt needle was used and in the second case one of the so-called Walker micropins made of platinum. In the first case the structure of the sclera as a whole was left intact. There was some hyperplastic scar tissue comprising the posterior part of the ciliary body. In the second case the effect was too destructive, resulting in a defect in the sclera into which part of the ciliary body herniated. This, of course, is not desirable.

The question then arises how many punctures should be made and how large an area has to be covered. The area to be covered can be seen in figure 3. It shows the relative location of the insertions of the recti muscles after E. Fuchs[10] and of the ora serrata according to Wagner's[5] findings. An area beginning from 2.5 to 3 mm. from the limbus to the ora serrata should be covered. Therefore on the inner side the punctures must extend back somewhat farther than the insertion of the internal rectus, on the inferior side just about beyond the insertion of the inferior rectus, and the same distance on the external side. If the punctures are applied to the upper part of the globe they should not extend quite as far as the insertion of the superior rectus. The coagulation needle should be left in the sclera a little longer than one second. I count 1, 2, 3 during the procedure. On the count of 1 I introduce the needle, on 3 I remove it. The needle should be under current throughout the procedure. Usually somewhat more than one third of the inferior circumference is treated. We tried to establish a relation between the number of millimeters of mercury of tension and the

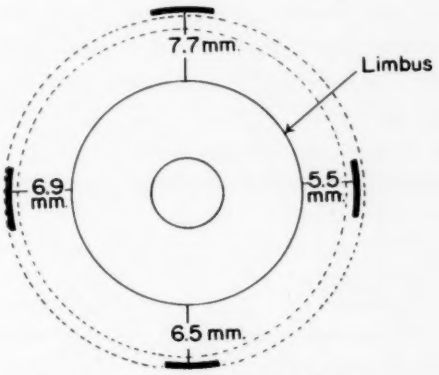

Fig. 3.—Area to be covered by cyclodiathermy puncture. The four wide black spaces indicate the distance from the limbus of the insertions of the rectus muscles. The parallel circles of broken lines indicate the distance from the limbus of the ora serrata, which is variable—5 to 7 mm. on the internal side and 6 to 7.5 mm. on the external, inferior and superior side.

9a. This needle is manufactured by V. Mueller & Co., 408 South Honore Street, Chicago 12, Ill.

10. Fuchs, E.: Beiträge zur normalen Anatomie des Augapfels, Arch. f. Ophth. **30** (pt. 4):1, 1884.

number of punctures. We are tentatively following the formula: number of millimeters of mercury of tension plus 30 equals the number of punctures required. However, never more than 80 punctures should be applied in chronic simple glaucoma.

SUMMARY AND CONCLUSIONS

1. Cyclodiathermy puncture as far as my experience with 16 cases of chronic simple glaucoma goes has proved to be a harmless procedure as deleterious complications have not developed in any case. (in 10 months)

2. Its influence on the tension and the general course of the disease is generally beneficial.

3. The lowering of the tension is of long duration, and there is much hope that by refining the technic and repeating the procedure when necessary permanent stabilization of the intraocular tension may be achieved even in those cases which show a tendency toward rise of tension after a certain time.

4. Cyclodiathermy puncture has certain definite advantages over other operations used for glaucoma simplex. It seems to work regardless of the type of glaucoma. No late infection is to be feared. No tendency toward stimulating the development of opacities of the lens can be demonstrated. No rapid deterioration after the operation in advanced cases, as frequently seen in some of the other procedures, occurs. It therefore may be applied safely in all stages of chronic simple glaucoma.

5. As shown in this study cyclodiathermy puncture is effective also for the Negro and may well become the method of choice for the treatment of the severe disease in this race.

6. A careful observation of the technic as outlined is essential.

DIABETIC RETINITIS

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CHANGES IN FUNDUS OF EYE ASSOCIATED WITH DIABETES

The changes which are seen in the fundus of the eye in cases of diabetes may be classified as follows:

I. Diabetic retinitis, or retinopathy proper
   1. Small, round and irregular hemorrhages
   2. Sharply defined, white exudates in the deeper layers of the retina
   3. Yellowish white, glistening deposits

II. Complicating elements in the ophthalmoscopic picture due to changes in the retinal vessels
   1. Changes due to aging and arteriosclerosis: irregular tortuosity of the vessels, irregularity of the lumen, widening of the light reflex, apparent compression of veins where crossed by arteries
   2. Changes due to contraction of small vessels in the course of the later stages of essential hypertension: a few small, irregular hemorrhages and an occasional cotton wool patch
   3. Changes due to obstruction of a large branch of the central vein: hemorrhages of all sizes in a sector of the fundus
   4. Changes due to episodal arteriospastic retinopathy in the course of the later stages of essential hypertension: edema of the retina and of the optic disk, cotton wool patches, other exudates and hemorrhages of all shapes and sizes

III. Changes found only in some cases of severe diabetic retinitis:
   1. Large, massive hemorrhages in the retina and in the vitreous
   2. Proliferation of numerous new vessels with connective tissue formation in the retina and in the vitreous

These various hemorrhages and exudates seen in the fundus of the eye present the first problem, that of diagnosis: What constitutes diabetic retinitis, or retinopathy proper? It is obvious that the changes in the vessels and the hemorrhages and exudates secondary to them which I have placed in group II cannot be due to diabetes. Aging and arteriosclerosis of the retinal vessels occur in advanced age in nondiabetic persons. Contractions of small vessels, obstruction of vascular branches and episodal arteriospastic retinopathy occur in the later stages of essential hypertension in persons without diabetes. The hemorrhages and exudates which are the result of such changes are, therefore, not due to the diabetes. However, diabetes is foremost a disease of middle and advancing age and so is essential hypertension, and both diseases are of frequent occurrence. It is natural, therefore, for these vascular changes and their consequences to occur in the course of diabetes, but there is not necessarily any causal relation between such changes and the diabetes. Moreover, these changes do not occur in young diabetic patients who do not have essential hypertension and do not show aging and arteriosclerosis of the retinal vessels. The only problem that these vascular changes present in relation to diabetes is the relative frequency of their occurrence in diabetic and in nondiabetic persons. I know of no satisfactory statistics which give the relative frequencies of arterial hypertension, aging and arteriosclerosis of the retinal vessels, contractions of small vessels, obstruction of branches of the retinal vessels and episodal arteriospastic retinitis in the various age groups of diabetic and of nondiabetic persons. Such statistics, if they are to have any value, will have to include large groups of cases and will have to consider the various degrees of severity of the diabetes and its duration, and a number of other factors. So far no such statistics are available.

Diabetic Retinitis or Retinopathy.—With the elimination of the vascular changes, there are left the hemorrhages and exudates in group I: (1) small, round and irregular hemorrhages; (2) sharply defined, white exudates in the deeper layers of the retina, and (3) yellowish white, glistening deposits.

The hemorrhages are situated mainly in the area between the upper and the lower temporal vessels of the retina and in the region surrounding the optic nerve head and may extend to the

Read at a meeting of the Clinical Society of Ophthalmology, New York, March 5, 1945.

periphery. Most of these hemorrhages are small, round and deeply situated, but superficial radial and irregular hemorrhages are also seen. The exudates are small and white, with sharp margins. They are discrete or confluent, forming all kinds of figures, including circinate ones. They are situated in the deep layers of the retina behind the retinal vessels. Their pathologic substratum is a deposit of hyalin mixed with lipid. The glistening, yellowish white exudates vary in size from a pinpoint to large irregular masses and are due to accumulations of cholesterol.

The small, round and deep hemorrhages constitute the most characteristic feature of diabetic retinitis. They do not stand in any relation to the complicating vascular changes of group II. In their characteristic form they occur only in diabetes, and in no other disease that I know of. When these hemorrhages are seen in the fundus of the eye, diabetes can be assumed to be present in practically every case. When the small white exudates and the glistening deposits are also seen, the complete picture of diabetic retinitis is present. This characteristic picture does not occur in any other disease. It is found not only in middle-aged and elderly but in young diabetic patients and may be present without any complicating vascular changes. In the discussion following the presentation of this subject by Dr. Sanford Gifford before the New York Diabetic Association in 1943, one of the speakers said that "retinal hemorrhages are found in some persons who are perfectly normal in every other respect." This is not so. Retinal hemorrhages are always pathologic, and small, deep and round hemorrhages are found only with diabetes. The relative frequency with which they are found in diabetic persons varies with the different investigators. Waite and Beetham [1] found deep retinal hemorrhages in 18 per cent of 3,915 visible fundi. The percentage varied with the duration of the diabetes, from 5.7, when the duration was only one year, to 58.9, when the duration was over fifteen years. I venture to state that the frequency would be still higher were the tiny hemorrhages more diligently sought for. As a feature of diabetes the ophthalmoscopic picture is of importance, for it is at times found on routine examination when the hyperglycemia is still below the threshold level for the excretion of dextrose in the urine.

Severe Retinal Complications.—I have placed the changes which complicate some cases of diabetic retinitis in group III. First of these are the retinal and preretinal large, and even massive, hemorrhages, which occur repeatedly and rupture into the vitreous. They do not occur in all cases of typical diabetic retinitis but appear only in a limited number. Such hemorrhages quickly destroy vision. They are difficult of absorption, and they are sometimes replaced by retinitis proliferans. Such hemorrhages arouse the suspicion that diabetes is present, even when they do not allow a good view of the fundus. They nullify the good results of a cataract extraction properly performed.

The second complication appears only in a small number of cases of diabetes, but it occurs only in this disease and is characteristic of it. There are seen in the fundus numerous fine, newly formed vessels covered by a thin, delicate, veil-like connective tissue. The vessels, with their covering of connective tissue, project into the vitreous in brushlike form or intertwined in various configurations. In a case seen at the New York Eye and Ear Infirmary the veil of tissue projected into the vitreous for about 8 D. and contained within its meshes a fine network of vessels. This formation of new vessels and connective tissue occurs without massive hemorrhages into the vitreous and differs in appearance from the proliferating connective tissue which follows the partial absorption of a hemorrhage in the vitreous. Although a number of such cases have been seen at the New York Eye and Ear Infirmary, their occurrence is not frequent. Hanum's [2] article contains excellent colored illustrations, and in Klien's [3] there are photographs and drawings showing the development of these vessels and their connective tissue support.

PATHOGENESIS OF DIABETIC RETINITIS

The second problem of diabetic retinitis is that of the pathogenesis of the small round hemorrhages, of the exudates, of the massive hemorrhages which rupture into the vitreous and of the new formation of vessels. The pathogenesis of the exudates is perhaps the easiest to explain. Deposits of hyalin and lipid occur in any tissue which suffers from insufficient nutrition and inadequate oxygen supply. Such a condition must be present in the retina in the areas where the exudates are found. Primarily the concern is with the small, deeply situated, round and irregular hemorrhages. There is no doubt that these hemorrhages occur by diapedesis through the

1. Waite, J. H., and Beetham, W. P.: The Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367 (Feb. 28); 429 (March 7) 1935.

2. Hanum, S.: Diabetic Retinitis, Acta ophth., 1938, supp. 16, p. 3.

3. Klien, B. A.: Retinitis Proliferans: Clinical and Histologic Studies, Arch. Ophth. **20**:427 (Sept.) 1938.

walls of the capillaries. The question is: What is there in diabetes which causes small hemorrhages by diapedesis into the retinal tissue?

There are certain well defined principles in pathology concerning the passage of blood through the capillary wall. When, for any reason, the capillaries are dilated, with a contraction or relative narrowing of the artery above, there is slowing of the blood flow in the capillaries, a condition of prestasis. The capillary wall becomes soft; openings form in it which permit the passage of red blood corpuscles, and these openings then close. Small hemorrhages in the retina, such as are typical of diabetic retinitis, can occur only in this manner. That there is in the retina a chronic prestatic condition, with slowing of the circulation in the capillaries, is also shown by the hyalin and lipids, which indicate a disturbed nutrition of the retinal tissue. The question then is: What is there in diabetes which causes a prestatic condition in the capillaries of the retina with resulting small hemorrhages?

There are a number of elements in the occurrence of the small hemorrhages of diabetic retinitis which must be kept in mind. They occur in young, as well as in middle-aged and old, persons. They have no relation to the vascular changes enumerated in group II. They occur with severe diabetes, as well as with the mild form. In fact, they occur frequently with long-standing mild diabetes, and they are at times discovered before the presence of glycosuria is known to the patient. If, therefore, one is to relate the prestatic condition of the retinal capillaries to the diabetes, it is the mild form of diabetes which one must consider—the moderate hyperglycemia, with slight secondary nutritional changes and without the terrific depletion of carbohydrate in the liver which results in secondary metabolic changes. How does a patient with such a mild form of diabetes differ from a normal person?

As I understand it, diabetes is a condition in which the organism is unable to maintain the normal blood sugar level, which is approximately 80 to 90 mg. per hundred cubic centimeters. If the maximum upper limit of normal is considered as about 110 mg., a continuous blood sugar level above this value, say from 130 to 160 mg., with or without glycosuria, constitutes mild diabetes. In a case of diabetes of this type, the lability of the blood sugar level is greater than normal, and the dextrose tolerance curve after the ingestion of carbohydrates is characteristic of diabetes. It is in such a case that the typical small hemorrhages are likely to occur. It must be remembered that in such a case, before the diabetes is even accidentally discovered, many years have passed, with the level of dextrose in the blood rising only gradually to 120, 140, 150 and 160 mg. per hundred cubic centimeters, until eventually glycosuria is noted. A patient with such a moderate degree of hyperglycemia differs in no manner from a nondiabetic person save in the lessened ability to regulate the blood sugar level. It is, therefore, in my opinion, the continuous moderate hyperglycemia lasting over years which stands in some causal relation to the production of a prestatic state in the capillaries with the resulting small hemorrhages. This is as far as I can go in attempting to explain the pathogenesis of diabetic retinitis. And this is as far as any one can go unless one would rather assume as a cause of the hemorrhages the presence of toxic substances which cannot be found or a deficiency of unknown vitamins, which so far have not been discovered, or attribute the hemorrhages to some of the vascular conditions mentioned in group II, which obviously have nothing to do with the typical hemorrhages of diabetic retinitis.

The attempt to relate causally the continuous moderate hyperglycemia to the hemorrhages of diabetic retinitis does not, of course, solve the whole problem of the pathogenesis of diabetic retinitis. Just how the hyperglycemia produces the prestatic condition in the capillaries of the retina I do not know. There also remains the question why the hemorrhages are not found in every case of diabetes, although they are probably present more frequently than any statistics indicate.

On the supposition that the hyperglycemia is the responsible factor, the massive hemorrhages which rupture into the vitreous can be assumed to be due to an aggravated form of prestasis. But why such an aggravated form occurs in only a limited number of cases of diabetic retinitis I do not know.

There still remains the necessity of explaining the occurrence of the newly formed vessels in some cases of diabetic retinitis. I know of no satisfactory explanation, unless perhaps the slowing of the circulation in a large number of capillaries at one time and in one area supplies the stimulus for the formation of new vessels.

TREATMENT OF DIABETIC RETINITIS

The third problem of diabetic retinitis is that of treatment. I know of no means which will prevent the occurrence of retinal hemorrhages in cases of diabetes or cause them to disappear when they have occurred. Usually the ophthalmologist

advises that the patient submit to a careful regimen of diet and insulin prescribed by his attending physician. Most ophthalmologists feel that the blood sugar should be kept as close to the normal level as possible. However, it is doubtful whether it is possible by any means to keep the blood sugar of any diabetic patient at the normal level of 80 to 90, or even 100 mg. per hundred cubic centimeters. Most physicians are quite satisfied when the blood sugar can be kept at about 130 to 150 mg. This level represents still a continuous mild hyperglycemia, just the condition which I think is responsible for the prestatic condition in the capillaries of the retina, with the resulting hemorrhages.

SUMMARY

Diabetic retinitis, or retinopathy, is an easily recognizable ophthalmoscopic entity characterized by small, round and irregular hemorrhages; sharply defined, white exudates in the deeper layers of the retina, due to hyalin and lipids, and yellowish white, glistening exudates, due to deposits of cholesterol.

The ophthalmoscopic picture is at times complicated by changes in the retinal vessels and their consequences, such as aging, arteriosclerosis, contraction of small vessels, obstruction of a venous branch and episodal arteriospastic retinopathy. There is no causal relation between these changes and those of diabetic retinitis.

Some of the cases of severe diabetic retinitis are characterized by large retinal hemorrhages which rupture into the vitreous. A few cases are also characterized by the proliferation in the retina and the vitreous of newly formed vessels, which are covered by a connective tissue layer. This form of retinitis proliferans differs in its appearance and its genesis from the retinitis proliferans following the partial absorption of a hemorrhage in the vitreous.

It is my opinion that in its pathogenesis diabetic retinitis stands in close relation to the continuous hyperglycemia which is in all probability responsible for the condition in the capillaries resulting in hemorrhages.

239 Central Park West.

REVALUATION OF HERBERT'S FLAP OPERATION FOR GLAUCOMA

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Lieutenant Colonel H. Herbert [1] of the Indian Medical Service contributed many splendid articles on the surgical treatment of glaucoma from 1903 to 1934. Like most ophthalmic surgeons of his day, he expressed himself in positive terms, stating at each writing that he had found a final solution for the treatment of glaucoma. A review of his contributions indicates that he discarded one discovery for another, leaving the reviewer with the impression that his accumulated experience compelled him to change his technic. He was one of the early pioneers advocating the use of the iris inclusion operation. But one of the outstanding methods which he so colorfully described as a future cure for glaucoma seems to have been abandoned in favor of more popular methods.

It is my purpose to rededicate his well known trapdoor or flap operation devised initially for

Fig. 1.—A narrow Graefe knife.

absolute glaucoma. In the *Transactions of the Ophthalmological Society of the United Kingdom,* of 1907 and 1910, Herbert described a rectangular trapdoor operation having as its basic principle the drainage of fluid from the interior of the eyeball through an opening in the sclera, in the anterior segment, to the subconjunctival space. Using a narrow Graefe knife (fig. 1), he made an incision in the sclera 2 mm. long and about 1.5 mm. from the corneal margin in the lower outer quadrant of the globe (fig. 2). From the two ends of this small incision, two shorter forward cuts were made to the limbus by turning the edge of the same narrow blade forward and sawing carefully to avoid puncturing the iris, in the emptied anterior chamber. He thus created a small rectangular flap or tongue of corneoscleral tissue, which was cut subconjunctivally with its base at the limbus (fig. 5). At a later period, Herbert repeated this operation in the upper outer quadrant of the eye (fig. 6). In a later report he moved the sclerotomy opening to the midline (fig. 4).

In his various reports, one is impressed by the many changes in the technic of performing this simple operation. For those who are interested in historical aspects, I refer to the original articles.

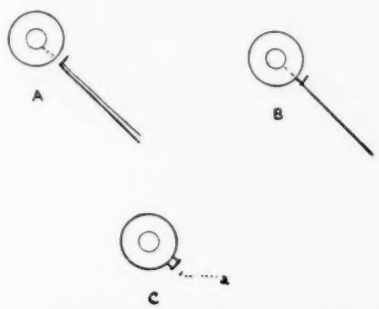

Fig. 2.—The earlier operation; *a,* conjunctival puncture.

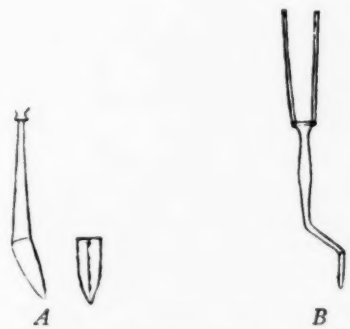

Fig. 3.—*A,* Syms iridectomy knife; *B,* Taylor's cataract knife, modified.

Regardless of the instruments used (fig. 3) and the delicate technic involved, there stands out conspicuously the underlying principle of the operation, namely the utilization of the trapdoor in the sclera which would serve as a continuous but slow drainage ditch siphoning the aqueous from the anterior chamber to the outside of the eye, under the conjunctiva.

Read at the meeting of the College of Physicians, Philadelphia, Section on Ophthalmology, March 15, 1945.

1. Herbert, H.: Tr. Ophth. Soc. U. Kingdom **23:** 324, 1903; **39:**220, 1919; **41:**239, 1921; Ophthalmoscope **5:**292, 1907; **9:**76, 1911; **11:**398, 1913; Brit. J. Ophth. **4:**216 and 550, 1920; **5:**183 and 417, 1921; **14:**433, 1930; **18:**142, 1934.

Colonel Herbert reports the result of his trapdoor operation on eyes already blinded by glaucoma. He claimed that he obtained good results in 5 cases out of 7.

Reading between the lines of his reports, I must deduce that he was satisfied with the term good result when he secured a reduction in the tension in absolute glaucoma without restoration of vision. He expressed the thought that the principle of the trapdoor operation might well be applied in the operation for primary glaucoma. It was this expression of opinion,

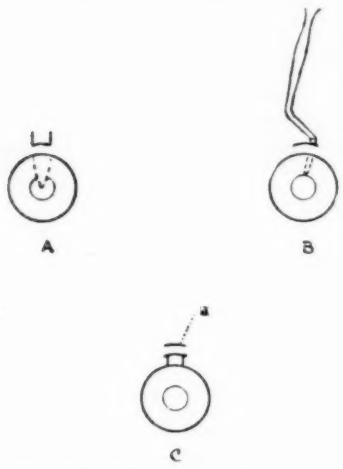

Fig. 4.—The "small flap" operation; *a*, conjunctival puncture.

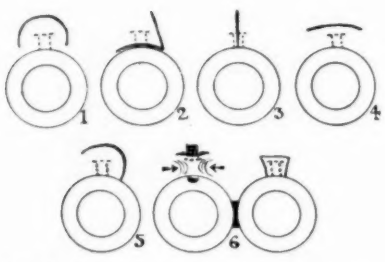

Fig. 5.—Various conjunctival incisions for Herbert's sclerotomy.

coupled with the rational hypothesis underlying the principle of this operation, that enticed me to pick up the threads where he left off.

I, too, like Herbert, operated in 7 cases in which the eyes were blinded by glaucoma, 2 of them secondary glaucoma, resulting from long-standing uveitis, and the remaining 5 primary glaucoma in the final stages of absolutism.

A MODIFIED TECHNIC OF TRAPDOOR OPERATION FOR ABSOLUTE GLAUCOMA

The technic is described as follows: An incision is made in the conjunctiva 8 mm. from the limbus. The conjunctiva is dissected in the same manner as when preparing for an Elliot trephine. Just 2 mm. below this point of incision, a scleral cut is made with a Graefe knife at least 4 mm. in length. The site of this incision need not be exactly at 12 o'clock but in a selected area where the anterior perforating ciliary vessels are least prominent. If the episcleral vessels cannot be avoided, then they must be sacrificed for the sake of the scleral incision. Several determined movements of the cataract knife may be necessary before the sclera is perforated. One need not fear the result of cutting the uveal elements beneath the sclera. Should they be cut inadvertently, no harm will result. At one end of the scleral incision, a blade of a sharp pointed scissors is entered between the sclera and the uveal coat while the other blade is on the sclera. A cut is made 2 to 3 mm. toward the cornea at an angle of 90 degrees. A similar cut is made at the opposite end of the scleral incision. The eye being under tension, there is an immediate prolapse of black uveal tissue. A spatula is then placed into the eyeball through

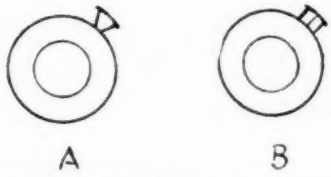

Fig. 6.—Modifications in the "small flap" operation.

the trapdoor opening and directed toward the anterior chamber in exactly the same manner as a cyclodialysis. While the spatula is still in position, it may be sufficiently depressed to allow escape of aqueous through the trapdoor. Following the removal of the spatula the conjunctival wound is closed by a continuous silk suture.

Instead of making a single trapdoor, a double sclerotomy may be performed, one in the upper nasal aspect and the second in the upper temporal aspect. Such a double opening is desirable in glaucoma in which the intraocular tension is very high and is attended by excruciating pain. The single trapdoor may be reserved for those cases in which light perception has been retained, and there exists hope of obtaining some restoration of vision, even though it be very slight.

I shall here report 2 cases in which the operation was used and which are very impressive.

REPORT OF CASES

CASE 1.—R. B., a woman aged 25, in 1940 had papillitis of the left eye from which she presumably recovered. In 1941, examination revealed a postpapillitic optic atrophy of the same eye. In January 1944, she con-

sulted me because of pain in the left eye with gradual loss of vision. The intraocular tension of both eyes was 40 —; visual acuity in the right eye was 5/5, and of the left eye, questionable light perception. There were the usual signs of chronic congestive glaucoma of the inflamed left eye with exacerbations of acute symptoms and glaucoma of the right eye with good vision, with changes in the fields characteristic of glaucoma.

Under miotics, the tension of the right, seeing eye was reduced to 21.5. In the left, blind eye the tension was 47; light perception was lost. With the development of absolute glaucoma in the left eye, pain became unbearable. The patient refused enucleation. A double Herbert operation was performed on April 3, 1944, one on the temporal and one on the nasal portion of the globe associated with cyclodialysis. There was complete cessation of pain, and the tension dropped to 15.

CASE 2.—E. B., a woman aged 49, in 1939 consulted me because of anterior uveitis of the left eye associated with pain and an intraocular tension of 35. Visual acuity was light perception. The tension of the fellow eye was 19, the visual acuity being 5/30 corrected by glasses to 5/9. She claimed that eleven operations had been performed on the sightless eye by the late Dr. L. Webster Fox over a period of years, temporary relief being obtained after each operation.

Fig. 7.—Trapdoor operation for absolute glaucoma. The sclerotomy is shaped like a staple, as shown in the artist's conception portrayed in the illustration.

A Herbert flap operation was performed Dec. 13, 1939 on the left, blind eye at a point 8 mm. from the limbus close to the insertion of the superior rectus muscle. A large trapdoor was made measuring 6 mm. horizontally and 4 mm. in a vertical direction at the extreme ends of the scleral incision. There was thus produced a U-shaped opening in the sclera through which uveal tissue extruded. The conjunctiva was closed in the usual manner over the trapdoor. The tension was gradually reduced, the last on record being 17 in the left affected eye on Dec. 8, 1944. The visual acuity with a minus 6.5 lens was 5/30. An area of chorioretinal atrophy in the inferior temporal quadrant was noted.

In this instance, the Herbert operation succeeded in establishing a point of drainage between the uveal coat of the eye and the subconjunctival space. It is now known that the patient had an acute localized choroiditis associated with secondary glaucoma. It is also now known that the Herbert operation established an avenue of escape for accumulated fluids from the posterior segment of the eyeball.

I am presenting also a photograph (fig. 7) of the eyes of a patient who refused surgical intervention for chronic congestive glaucoma. Only when he became totally blind, and the right eye became painful did he submit to surgical procedure. A Herbert operation was performed on the right eye which still had light perception. He now has light perception with marked reduction in intraocular pressure, the record of Nov. 14, 1944 being: right eye, tension 25, left eye, not operated on, 41.

CONCLUSIONS ON HERBERT OPERATION

I am satisfied that enucleation should be performed on all painful blind eyes associated with increased intraocular pressure. There are circumstances in which the patient does not agree to surgical removal. Only in those instances in which blindness results from chronic uveitis or as a result of a primary glaucoma do I believe that the Herbert operation should be performed to relieve pain and to satisfy the patient's whim of retaining a dead eyeball.

POSSIBILITIES OF HERBERT'S FLAP OPERATION

Herbert proposed that the trapdoor operation may be effective in all cases of primary glaucoma. That was in 1910. In later publications, 1920 and 1921, he reported that he and his associates performed the sclerotomy for primary and secondary glaucomas as it was introduced in 1907. He concluded that the sclerotomy was valuable when miotics failed to hold the tension. In 1934, he reported a series of iris inclusion operations, indicating that the anterior sclerotomy had failed to serve his purpose in all cases.

I believe, however, that Herbert was persuaded by the popularity of iris inclusion operations. In reviewing the various types of operations for glaucoma, principally the primary type, I find that Herbert did make an extremely important contribution in the small flap operation. I am speaking, however, of the principle underlying the operation rather than of the surgical procedure itself. I find that this principle may be further modified by moving the area of sclerotomy to a point corresponding to and beyond that space in the sclera covering the ciliary body.

At present, the common location for operation for glaucoma is limited to the corneoscleral margin at a point where the canal of Schlemm has already been occluded and at the point where serious accidents occur by the operation itself.

If one were to accept the theory that acute and chronic congestive glaucoma are attended by enlargement of the ciliary body and a swelling of the entire choroid coat, then one must also accept the hypothesis that the pathologic process

in the anterior segment of the eye in the region of the canal of Schlemm, with all its implied connections of iridocorneal disease, and the general advancing of all the ocular tissues forward are the result of the increased fluid content of the vitreous chamber segment.

If, again, the origin of acute glaucoma is in the vitreous chamber segment, it seems equally logical that the new exit of fluids should be made in the silent portion of the eyeball, rather than at the corneal margin.

The same holds true for chronic simple glaucoma which has as its basic pathologic conditions arteriosclerosis and fibrosis of the tissues of the eyeball. If one holds to the theory that the canal of Schlemm is so sclerosed and fibrotic that it is no longer an exit for fluids then it is likewise true that the new exit for these fluids should not be in the obstructed angle but in the silent areas of the eyeball.

Herbert originally made his anterior sclerotomy 1.5 mm. from the limbus. Later, he agreed to advance it to 2, 3 and 4 mm. My contribution to the Herbert operation is a further shifting of the exit in the sclera 4 to 8 mm. from the limbus, producing a trapdoor in the region of the eye corresponding to the location of the ciliary body and immediately beyond, where the fluids are excreted and where they may be evacuated at their source. This area is approximately 6 mm. from the limbus. It is my opinion that the Herbert operation can be reenforced in value if performed at a new location situated away from the dangerous area of the eye which has already been damaged by increased pressure. The operation can be performed without serious trauma and certainly without the complications common to the trephine, inclusion operations and basal iridectomy. The trapdoor is not a fistulous opening. It is closed with a layer of uveal tissue which is noted as a black U-shaped area beneath the conjunctiva. This uveal tissue acts like spongy weather stripping through which fluids are exchanged between the inside and the outside of the eyeball. It serves as a wick just as in the iris inclusion operations. The operations can be repeated at different locations should ocular tension return.

Of course my experience is limited to 2 cases of uveitis and to 5 of absolute glaucoma. Until I have been able to report convincingly on the trapdoor operations in early primary glaucoma, I must hold my judgment in abeyance. However, ideas must precede performance. I am presenting Herbert's principle of the trapdoor operation, some distance away from the corneoscleral margin, as an idea for future guidance in the surgical treatment of primary glaucoma.

PENETRATION OF PENICILLIN INTO THE EYE

FURTHER STUDIES

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Studies by Struble and Bellows [1] and Leopold and LaMotte [2] on the penetration of penicillin into the eye after topical and systemic use were carried out with commercial preparations, and the concentrations obtained in various parts of the eye were expressed in Oxford units. A direct comparison of their results and those published by this laboratory [3] is not possible, since in our experiments a relatively crude preparation of penicillin was applied. The strain of Penicillium notatum used was grown in the medical department of the Presbyterian Hospital under the supervision of Dr. Gladys Hobby and extracted in the laboratory of Dr. Karl Meyer, of the Department of Ophthalmology; titration according to the Oxford method was not done. In the same study, the penicillin activity in the aqueous and vitreous fluids was determined by means of the Fleming dilution method, and the concentrations were given in micrograms of penicillin per cubic centimeter. Although the results clarified the relation of the three types of topical application in the rabbit's eye, it was thought advisable to repeat and to extend several series of experiments using solutions of commercial salts and to estimate the penicillin activity of the ocular fluids by the Oxford cup method and the Fleming dilution technic, and that of the tissues of the eye by the Oxford cup method. The determinations of penicillin in the latter tissues were made in conformity with the work of Struble and Bellows. Three local methods, designed to introduce comparatively high concentrations of drugs in the anterior segment of the eye, were tested on rabbits and the results compared: subconjunctival injection, iontophoresis and the application of cotton packs saturated with a solution of penicillin. The penetration of penicillin into the human eye after two types of topical application was estimated in several suitable cases to procure information on the extent to which the results of experiments on rabbits are applicable to the human eye.

This study was supported by the Knapp Memorial Foundation.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

The penicillin for these experiments was released by the Committee on Therapeutics and Other Agents, Division of Medical Sciences, National Research Council. Preparations from two large pharmaceutical companies were used.

1. (*a*) Struble, G. C., and Bellows, J. G.: Studies on the Distribution of Penicillin in the Eye and Its Clinical Application, J. A. M. A. **125**:685 (July 8) 1944. (*b*) Bellows, J. G.: Penicillin Therapy in Ophthalmology, Am. J. Ophth. **27**:1206 (Nov.) 1944.

2. Leopold, I. H., and LaMotte, W. O., Jr.: Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, Arch. Ophth. **33**:43 (Jan.) 1945.

3. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye, Arch. Ophth. **31**:1 (Jan.) 1944.

SUBCONJUNCTIVAL INJECTION

Technic.—One-half cubic centimeter of a solution of commercial sodium penicillin containing 5,000 Oxford units of penicillin per cubic centimeter was injected subconjunctivally. After local anesthesia with 0.1 per cent nupercaine hydrochloride, half the amount was injected beneath the upper part of the bulbar conjunctiva and the remainder beneath the lower part. One, two, four and six hours later, aqueous and vitreous fluids were withdrawn; the cornea and the iris with the ciliary body were dissected at the one, two and four hour intervals. The amount of penicillin in the aqueous was generally determined in appropriate dilutions by means of the Oxford cup and Fleming dilution methods. The cornea and the iris with the ciliary body were weighed and ground with ignited quartz sand and a phosphate buffer solution (p_H, 6.7 to 7.0). which was also used for the washing of the mortars, pestles and weighing bottles. The extracts and washings were combined in a centrifuge tube and diluted to twenty times the weight of the respective tissue. The tubes were centrifuged, and quadruplicate samples of the supernatant fluid were used for the determination of penicillin by the Oxford cup method. Whenever possible, the samples were kept on ice during the various steps of processing. Each experiment was repeated three to eight times.

Results.—The subconjunctival accumulation of fluid was commonly yellow one hour after the injection. At this time the amount of penicillin in the aqueous (table 1) varied from 0.75 to 1.0 Oxford unit per cubic centimeter as determined by the dilution method and from 0.68 to 1.4 Oxford units per cubic centimeter as determined by the cup method. The averages for the two types of determination were in close agreement, 0.91 and 0.93 Oxford unit, respectively, per

cubic centimeter. The vitreous fluid exhibited a slight degree of penicillin activity in 1 of 5 instances. The figures for the cornea are given in Oxford units per gram wet weight. The penicillin content of the individual corneas ranged from 6 to 12 per cent of the average given in the table for 1 Gm. wet weight. The quantity of penicillin in the corneas varied from 32.8 to 75.5 Oxford units, with an average of 53.2 Oxford units, per gram wet weight. The iris with the ciliary body also showed variations in penicillin content, that is, from 7.1 to 23.1 Oxford units, with an average of 14.3 Oxford units, per gram wet weight.

TABLE 1.—*Concentration of Penicillin in the Aqueous, Cornea and Iris with Ciliary Body After Subconjunctival Injection of 0.5 Cc. of a Solution of Commercial Sodium Penicillin Containing 5,000 Oxford Units of Penicillin per Cubic Centimeter*

	Concentration, Units/Gm. or Cc.					
	1 Hour		2 Hours		4 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous.....	0.68	1.0	1.04	1.6	0.5	...
	0.8	0.8	1.14	0.4	0.51	...
	1.4	1.0	0.7	0.5	0.2	...
	0.82	0.8	0.63	0.5	0.26	...
	....	0.75	....	...	....	0.2
	....	0.75	....	...	....	0.4
	....	....	....	...	....	0.2
	....	....	....	...	....	0.1
	....	....	....	...	....	0.1
Average.....	0.93	0.91	0.88	0.75	0.37	0.17
Cornea.....	75.5	....	30.6	...	Trace	...
	61.4	....	57.5	...	Trace	...
	43.1	....	23.7	...	Trace	...
	32.8	....	27.8	...	Trace	...
Average.....	53.2	....	34.9			
Iris with Ciliary Body	23.1	....	Trace	...	Trace	...
	12.6	....	Trace	...	Trace	...
	7.1	....	Trace	...	Trace	...
Average.....	14.3					

The bulging of the conjunctiva was but little decreased two hours after injection and was still marked at the four hour interval. The quantity of penicillin in the aqueous, 0.88 Oxford unit per cubic centimeter, was slightly less after two hours than after one hour. No measurable amount of penicillin was detected in the vitreous fluid. In the second hour after the injection the cornea lost 30 per cent of the penicillin present after the first hour. At this time the iris with the ciliary body exhibited only traces of penicillin activity. The decrease in the penicillin concentration in the examined fluids and tissues continued in the period that followed; only traces were found in the cornea after four hours and only 1 of 6 samples of aqueous contained a detectable amount of penicillin after six hours.

Comment.—A previous study on the penetration of alkaloids [4] into the eye showed that comparatively small quantities of salt solutions enter the aqueous after subconjunctival injection. This observation appeared to be confirmed by the investigations of Struble and Bellows on subconjunctival injection of penicillin. The concentrations in the aqueous and in the iris with the ciliary body in the present study were similar to those given by Struble and Bellows, but there was considerable difference in the amounts of penicillin determined in corneal extracts. The diversity may be explained by variations in the technic—that is, in the placing of the depot, in the amount of the solvent and in the time of sampling. The vitreous demonstrated a trace of penicillin activity in 1 instance and none in 5 instances, whereas Struble and Bellows reported the presence of 1.9 Oxford units per cubic centimeter of vitreous fluid. The value of this figure is uncertain in view of the authors' statement, "Caution must be exercised in interpreting results since the number of experiments performed was small." From the present series of experiments on rabbits it can be concluded that the penicillin content of the cornea and the iris with the ciliary body is considerable, whereas the concentration in the aqueous is low and that in the vitreous negligible.

The conspicuous bulging of the conjunctiva visible for four to six hours was apparently due to the accumulation of tissue fluid, since the concentration of penicillin in the aqueous and tissue extracts decreased steadily after the first hour. There was no indication that any of the examined fluids and tissues retained penicillin for more than six hours.

The solution of penicillin injected contained 5,000 Oxford units per cubic centimeter. It is questionable whether solutions of this strength can be employed subconjunctivally in the human eye without producing a severe reaction. In 2 patients a solution containing 2,000 Oxford units per cubic centimeter caused obvious discomfort.

IONTOPHORESIS

Technic.—Two solutions of commercial sodium penicillin containing 1,000 and 5,000 Oxford units per cubic centimeter, respectively, were prepared in a 0.9 per cent solution of sodium chloride. The technic for iontophoresis was the same as that described in previous articles [5]; that is, a galvanic current of 2 milliamperes was applied from the cathode for five minutes with the

4. von Sallmann, L.: Iontophoretic Introduction of Atropine and Scopolamine into the Rabbit Eye, Arch. Ophth. **29**:711 (May) 1943.

5. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426 (Oct.) 1943.

eye under local anesthesia, using the corneal route. Determination of the penicillin activity of the ocular fluids and tissue extracts was carried out with the same technic as that described in the experiments with subconjunctival injection and was extended to the lens. After dissection, the lens was dipped in isotonic solution of sodium chloride to wash off adhering aqueous; it was then weighed, ground with quartz sand and diluted to four times its weight with buffer solution. In the series in which solutions containing 1,000 Oxford units per cubic centimeter were applied, the determinations were confined to a one hour interval. In the series with a solution of 5,000 Oxford units per cubic centimeter, determinations were made one, four, six and eight hours after iontophoresis.

Results.—A single iontophoretic application of the solutions containing 1,000 to 5,000 Oxford units per cubic centimeter did not cause damage of the corneal epithelium except for a transient haze. One hour after iontophoresis with a solution of 1,000 Oxford units per cubic centimeter, the average penicillin content of the aqueous for 6 experiments was 3.3 Oxford units per cubic centimeter as determined by the dilution method and 2.2 Oxford units as determined by the Oxford cup method. The average concentration of penicillin in the extract of the cornea was 103.5 Oxford units per gram wet weight. The extract of the iris with ciliary body had a concentration of 54.9 Oxford units per gram wet weight in 1 instance. In 4 instances the twentyfold dilutions contained only traces of penicillin. Neither the vitreous fluid nor the diluted lens extract showed any penicillin activity.

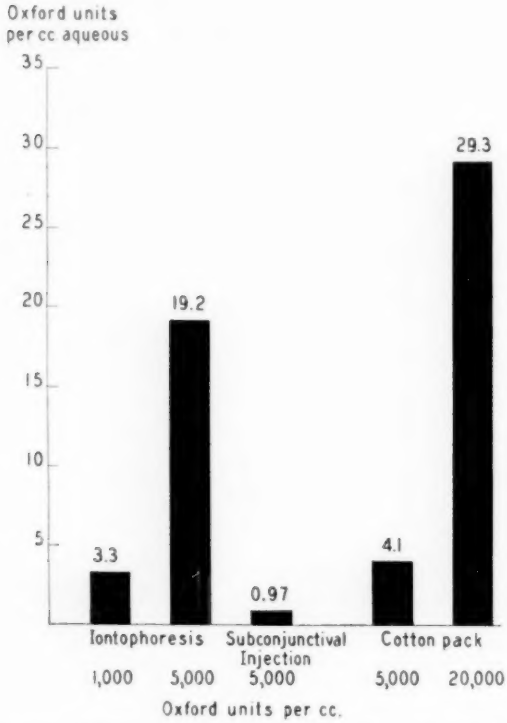
With the application of a solution of penicillin containing 5,000 Oxford units per cubic centimeter the concentrations of penicillin in the aqueous were greatly increased (table 2). After one hour an average of 19.2 Oxford units per cubic centimeter was determined by the dilution method; the cup method gave considerably lower readings, with an average of 9.9 Oxford units per cubic centimeter. Possible explanations for the difference in the results with the two methods will be given later. In the cornea the concentration varied from 201.6 to 357.5 Oxford units per gram wet weight. The average concentration in the ciliary body was 65.9 Oxford units, with variations between 40.4 and 85.4 Oxford units, per gram wet weight. The undiluted vitreous fluid and the lens tissue diluted four times its weight again did not contain measurable amounts of penicillin.

There was a continuous decrease in the concentration of penicillin in the aqueous within the seven hours following the first determination. The average of 2.97 Oxford units per cubic centimeter determined after four hours was approximately one sixth of the amount determined after one hour. At the eight hour interval an average of 0.14 Oxford unit per cubic centimeter was estimated. The depletion of the penicillin in the anterior part of the uvea was similar to that in the aqueous. The corneal extract contained after four hours about one third of that after one hour and slightly less after six hours. A steep decline in the concentration of penicillin in the cornea occurred after this time.

TABLE 2.—*Concentration of Penicillin in the Aqueous, Cornea and Iris with Ciliary Body After Iontophoresis with a Solution of Commercial Sodium Penicillin Containing 5,000 Oxford Units of Penicillin per Cubic Centimeter*

	Concentration, Units/Gm. or Cc.							
	1 Hour		4 Hours		6 Hours		8 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous	11.84	19.2	3.44	2.4	0.48	....	0.17	....
	9.12	19.2	1.8	3.25	0.40	....	0.19	....
	8.68	19.2	1.9	3.25	0.44	....	0.07	....
	10.52	19.2	3.5	....	0.33	....	0.13	....
	9.44	19.2	3.7	....	0.41	....	....	—
	....	....	....	....	0.44	0.44	....	—
	....	....	....	....	....	0.1	....	—
	....	....	....	....	....	0.375	....	—
	....	....	....	....	....	0.5	....	....
Average	9.92	19.2	2.87	2.97	0.42	0.35	0.14	....
Cornea	357.5	....	55.8	....	104.0	....	—	....
	241.0	....	91.2	....	153.1	....	Trace	....
	201.6	....	110.7	....	71.9	....	—	....
	....	....	94.3	....	70.1	....	—	....
	....	....	89.7	....	20.6	....	....	....
	....	....	....	....	20.3	....	....	....
Average	266.7	....	88.3	....	73.3	....	....	....
Iris with Ciliary Body	85.4	....	Trace	....	Trace	....	—	....
	70.9	....	Trace	....	Trace	....	—	....
	40.4	....	Trace	....	Trace	....	—	....
	....	....	29.8	....	—	....	—	....
	....	....	21.1	....	Trace	....	....	....
Average	65.9	....	....	....	—	....	....	....

Comment.—The preparation of penicillin employed in a previous study was found to cause considerable damage in a concentration of more than 2.5 mg. per cubic centimeter [3]; the damage may have been due to the alcohol with which the free acid of penicillin was treated in the process of converting it to sodium penicillin. The commercial sodium salt was tolerated by the rabbit eye in an approximate concentration of 11 mg. per cubic centimeter when a single iontophoretic application was given.[6] The same concentration was used in daily iontophoretic



Concentration of penicillin in the aqueous one hour after various methods of local application.

treatment of infections of the human eye without undue effect.

APPLICATION OF COTTON PACKS SATURATED WITH SOLUTIONS OF PENICILLIN

Technic.—Small pieces of absorbent cotton were soaked with 0.1 cc. of a solution of sodium penicillin. Two concentrations, 5,000 and 20,000 Oxford units per cubic centimeter, were employed. The higher concentrations were selected in conformity with the work of Struble and Bellows,[1a] who instilled solutions of similar strength. Local anesthesia was used to increase the permeability of the cornea, and brief ether anesthesia was also employed to permit the insertion of two mattress sutures at the lid borders. After the saturated cotton packs were placed in the lower fornix of the conjunctiva, the sutures were tied. With the exception of one series, the sutures and cotton packs were removed after one hour. The globes were enucleated at the end of one, four and six hours, respectively, and were rinsed with saline solution to remove penicillin remaining on the surface. The subsequent technic was the same as that described in the experiments with subconjunctival injection. In one series the packs were removed and the eyes enucleated after two hours. All experiments were repeated three to nine times.

Results.—One hour after the insertion of the cotton pack saturated with 0.1 cc. of a solution containing 5,000 Oxford units per cubic centimeter, the part of the conjunctiva with which it had been in contact was moderately edematous; no other change was noticeable. The average concentration of penicillin in the aqueous after one hour was 4.1 Oxford units per cubic centimeter (figure). The amount of penicillin determined in the cornea ranged from 260.5 to 401.9 Oxford units, with an average of 347.2 Oxford units, per gram wet weight. The penicillin content of the iris with the ciliary body was also high, ranging from 69.9 to 100.6 Oxford units, with an average of 85.0 Oxford units, per gram wet weight.

When the packs were kept in the conjunctiva for two hours, a definite increase of penicillin activity was noted both in the aqueous and in the cornea, and the depletion in the iris with the ciliary body was almost complete. Undiluted vitreous fluid did not show antibacterial activity at the intervals tested. Determinations at longer intervals were not carried out.

Cotton packs saturated with 0.1 cc. of a solution containing 20,000 Oxford units of penicillin per cubic centimeter were applied for one hour. The edema of the conjunctiva in these experiments was more pronounced than that described in the experiments with a solution containing 5,000 Oxford units per cubic centimeter. The conjunctiva, the subconjunctival tissue and the marginal area of the lower half of the cornea occasionally presented a yellow discoloration at the one hour period. In 2 instances there was a haziness of the lower segment of the cornea, probably due to slight displacement of the cotton pack. The amounts of penicillin determined at this time were excessive and far surpassed the readings obtained after various types of application with weaker solutions. As table 3 shows, the average concentration of penicillin in the aqueous was 29.3 Oxford units per cubic centimeter as determined by the dilution method and 23.7 Oxford units per cubic centimeter as determined by the Oxford cup method.

The corneal extract contained penicillin in such unexpectedly high concentrations that the dilutions in the first 4 experiments were not great enough to assure reliable readings. Later ex-

6. Higher concentrations were not used, in order to economize on the penicillin.

periments revealed an average of 1,728.9 Oxford units, with values from 1,107.7 to 2,535.2 Oxford units, per gram wet weight. The extracts of the iris with ciliary body also contained relatively large amounts of penicillin, ranging from 255.7 to 637.4 Oxford units, with an average of 465.1 Oxford units, per gram wet weight.

TABLE 3.—*Concentration of Penicillin in the Aqueous, Cornea and Iris with Ciliary Body After Application of a Cotton Pack Saturated with a Solution of Commercial Sodium Penicillin Containing 20,000 Oxford Units of Penicillin per Cubic Centimeter*

	Concentration, Units/Gm. or Cc.					
	1 Hour		4 Hours		6 Hours	
	Cup Method	Dilution Method	Cup Method	Dilution Method	Cup Method	Dilution Method
Aqueous	28.4	30.6	4.8	2.4	0.52	0.5
	25.2	30.2	5.7	3.2	1.44	1.0
	9.0	8.9	0.55	0.63	0.5	0.25
	14.0	17.8	3.6	2.5	0.52	0.5
	30.2	40.0	...	...	....	...
	35.2	40.0	...	...	....	...
	....	24.0	...	...	....	...
	....	24.0	...	...	....	...
	....	48.0	...	...	....	...
Average	23.7	29.3	3.7	2.2	0.75	0.56
Cornea	1,107.7	....	72.1	...	40.7	...
	1,661.7	....	97.8	...	51.2	...
	1,611.1	....	99.1	...	13.6	...
	2,535.2	....	....	...	14.5	...
Average	1,728.9	....	89.7	...	30.2	...
Iris with Ciliary Body	63.74	....	31.5	...	Trace	...
	479.3	....	50.4	...	Trace	...
	628.4	....	66.7	...	Trace	...
	414.6	....	....	...	....	...
	451.1	....	....	...	....	...
	254.7	....	....	...	....	...
	255.7	....	....	...	....	...
	599.4	....	....	...	....	...
Average	465.1	....	49.9	...	....	...

Despite the abundance of penicillin in various parts of the anterior segment, not more than a trace of it was found in the lens and none in the undiluted vitreous fluid. Four hours later the aqueous had an average concentration of 2.2 (dilution method) and 3.7 (Oxford cup method) Oxford units per cubic centimeter. The content of penicillin in the cornea dropped at this period to about one-twentieth, and that in the iris with the ciliary body to about one-tenth, the content after one hour. Traces of penicillin were again found in the diluted lens extract, but no penicillin was detected in the undiluted vitreous fluid. Depletion after six hours had advanced in the aqueous to an average of 0.56 (dilution method) and 0.75 (Oxford cup method) Oxford unit per cubic centimeter. The corneal extract was estimated to contain at this time approximately 30.2 Oxford units of penicillin per gram wet weight, and the diluted extract of the iris with the ciliary body showed only traces of penicillin.

Comment.—Large quantities of penicillin were obtained in the aqueous, cornea and iris with ciliary body when determinations were made immediately after the removal of the packs (20,000 units per cubic centimeter) which had been in place for one hour. These readings greatly surpassed those of Struble and Bellows, who applied an excess of solution containing 20,000 Oxford units of penicillin per cubic centimeter in the conjunctival sac of the rabbit and clamped the lids for a period of thirty minutes to three hours. The highest concentrations which they tabulated were as follows: aqueous, 15 Oxford units per cubic centimeter; cornea, 45 Oxford units per gram wet weight, and iris with ciliary body, 35 Oxford units per gram wet weight. Despite the high initial values achieved with the insertion of the packs, the depletion of penicillin was almost complete after six hours, as table 3 shows.

COMMENT ON EXPERIMENTAL INVESTIGATION

When a solution of penicillin containing 5,000 Oxford units per cubic centimeter was applied, the iontophoretic administration resulted in the highest concentrations of penicillin in the aqueous fluid (figure). This amount of penicillin was obtained one hour after ionization for five minutes whereas after subconjunctival injection and the insertion of the cotton pack the depots of penicillin remained in place for one hour. The cornea and the iris with ciliary body contained more penicillin after application of the pack. Although a dilution of the administered penicillin of course occurred, the subconjunctival fluid as well as the cotton pack were still yellow at the one hour interval.

The highest penicillin levels by far were observed after the cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter were applied for one hour.[7] The aqueous contained approximately 50 per cent more penicillin than after iontophoresis with a solution of penicillin having 5,000 Oxford units per cubic centimeter, and the cornea and iris with ciliary body contained five to eight times as much.

None of the methods of topical application secured more than traces of penicillin in the vitreous fluid and the lens. This observation strongly suggests that neither iontophoresis

7. Neely, J. C., and Cross, A. G.: Penicillin Lamellae in Eye Conditions, Lancet **1**:85 (Jan. 20) 1945. These authors suggested the use of lamellas containing penicillin in the eye. The results of studies on the penetration of penicillin into the eye from lamellas have not been reported.

through the cornea nor the administration of cotton packs nor subconjunctival injection will be effective in treatment of deep infections of the lens or vitreous. After a single iontophoretic application with a solution of penicillin containing 5,000 Oxford units per cubic centimeter, a bacteriostatic level of penicillin remained in the aqueous over a period of eight hours. The gradient of depletion was steeper in the experiments with cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter, so that the concentration in the aqueous after four hours was approximately the same as that following iontophoresis with a solution containing 5,000 Oxford units per cubic centimeter at the same interval.

The individual values within the single series of experiments were at considerable variance. Anatomic differences in rabbits' eyes and unavoidable inaccuracies in the technic of application may explain in part the diversity of the results. Also relatively inexact are the bioassay methods applied. In addition, the extraction and processing of the tissue fluids increase the limits of error far beyond those estimated by Florey for the cup method. This does not explain, however, the differences in several series in which the two types of penicillin determinations were made on the same sample of aqueous fluid. The divergence was most striking in the series in which a solution containing 5,000 Oxford units per cubic centimeter was applied iontophoretically (table 2, columns 1 and 2). The measurements with the Oxford cup method were taken at the upper end of the standard curve and are, therefore, less reliable than those obtained with the dilution method. Another explanation is suggested by the experiments of Chow and McKee,[8] who showed that penicillin combined with serum albumin to form a penicillin-albumin complex that possessed antibiotic activity. It is possible that the formation of such a complex in the aqueous, which is rich in protein after iontophoresis, interfered with the diffusion of the sample in the cup method. More experiments are planned, however, to demonstrate whether this factor accounts for the divergence of the comparable figures secured by the two methods of determination after iontophoresis.

PENETRATION OF PENICILLIN INTO THE AQUEOUS OF HUMAN EYES

Studies on the penetration of sulfonamide drugs into the eye have demonstrated that the results derived from experiments on laboratory animals, especially rabbits, can be applied to the human eye only with caution. Rabbit experiments were the basis for all of the present and previous investigations carried on in this laboratory, most of those of Bellows and Struble and those of Leopold and LaMotte concerning the penetration of penicillin into the eye. It was advisable, therefore, to estimate the amount of penicillin in the aqueous of suitable human eyes after topical administration. The examinations of aqueous were carried out on eyes which were to be enucleated. Instillations and application of cotton packs were selected as being least disturbing to the patient.

Technic.—After local anesthesia with tetracaine, 4 drops of a solution of commercial sodium penicillin containing 20,000 Oxford units of penicillin per cubic centimeter was instilled in 1 instance, and cotton packs saturated with 0.1 cc. of a solution of penicillin of the same strength were placed in the lower fornix in 3 instances. The eyes were patched until the withdrawal of the aqueous one to two hours later. The aqueous was appropriately diluted with phosphate buffer, and the penicillin content was determined by the Oxford method.

Results.—The following observations were made:

CASE 1.—L. N., aged 46, had a lesion diagnosed as a small circumscribed malignant melanoma above the disk. The anterior segment of the eye was normal. One and one-half hours after the insertion of the cotton pack the aqueous was estimated to contain 2.3 Oxford units of penicillin per cubic centimeter.

CASE 2.—M. S., aged 50, had a lesion diagnosed as a small malignant melanoma near the optic nerve. The anterior segment was normal. One hour after the insertion of the cotton pack no penicillin was detected in a fourfold dilution of the aqueous.

CASE 3.—A. G., aged 74, had a condition diagnosed as absolute glaucoma. A flat scar was present in the limbus after an Elliot operation (1934). The globe showed marked circumcorneal injection and was hard (tension plus 3). The cornea was slightly hazy and the anterior chamber shallow. One hour and fifteen minutes after insertion of the cotton pack, the aqueous was estimated to contain approximately 9 Oxford units of penicillin per cubic centimeter.

CASE 4.—F. O., aged 17, had a condition diagnosed as endophthalmitis following a perforating injury with an intraocular foreign body near the posterior pole of the globe. The eye showed intensive mixed injection, a cloudy cornea and a swollen and hyperemic iris. Two hours after the instillation of penicillin, the aqueous was estimated to contain approximately 0.6 Oxford unit of penicillin per cubic centimeter.

Comment.—Two observations on aqueous fluid from human eyes with normal anterior segments indicated that the values were more erratic than those secured in normal rabbit eyes. The average amount of penicillin in the aqueous was approximately one twentieth of that determined in rabbits. The negative result in case 2

8. Chow, B. F., and McKee, C. M.: Crystalline Penicillin and Human Plasma Proteins, Science **101**:67 (Jan. 19) 1945.

may have been caused by the reflex tearing due to the mechanical irritation.

The pathologic condition of the cornea probably explains the relatively high concentration of penicillin in the aqueous of the glaucomatous eye (case 3). The single instillation of 4 drops of a solution of penicillin containing 20,000 Oxford units per cubic centimeter, however, produced in the inflamed eye in case 4 a concentration of penicillin which was only about one-fifth that found by Bellows and Struble in the normal rabbit eye with the same technic. It is not feasible, therefore, to apply directly to the human eye the values tabulated by Leopold and LaMotte for the aqueous of rabbits with abraded or inflamed corneas and to conclude that instillations or the application of ointments can be substituted for iontophoresis or other vigorous procedures in the treatment of intraocular infections.

On the basis of in vitro experiments, the question arises again whether the attempts to increase the concentration of penicillin in eyes with intraocular infections are justified. Garrod[9] observed that the relatively impure commercial penicillin tested against Staphylococcus aureus was less active in high concentration than in low. He stated:

> The only good reason for using strong solutions in local treatment is to ensure that loss by escape, dilution, or absorption shall not permit the concentration to fall below the minimum level for full effect.

The data presented in this paper indicate that the conditions requiring the use of concentrated solutions exist in treatment of intraocular infections. If the initial level of the drug substantially exceeds the effective concentration, the presence of the minimal effective amount will be prolonged so that the deeper foci are more likely to be beneficially influenced. It should be stressed that the ratio between the concentration of the solution administered and the concentration of the drug determined in the aqueous was about 260:1 to 300:1 after use of the ionization method and about 660:1 to 1,200:1 after employment of the pack technic. Furthermore, it was apparent from a small number of studies that this ratio became even more unfavorable in the human eye. There is, therefore, a sound theoretic basis for preferring rigorous procedures in treating exogenous infections of the anterior segment of the human eye.

9. Garrod, L. P.: Action of Penicillin on Bacteria, Brit. M. J. **1**:107 (Jan. 27) 1945.

SUMMARY

1. A comparison of the results of subconjunctival injection, iontophoresis and application of cotton packs, using a solution of commercial sodium penicillin containing 5,000 units of penicillin per cubic centimeter, showed that the highest concentration was obtained in the aqueous by iontophoresis and in the cornea and the iris with ciliary body by the prolonged application of cotton packs. The lowest concentration of penicillin in the aqueous, the cornea and the iris with ciliary body was observed after subconjunctival injection.

2. Extremely high concentrations of penicillin were determined in the cornea and the iris with ciliary body after the application of cotton packs saturated with a solution of sodium penicillin containing 20,000 Oxford units of penicillin per cubic centimeter. The penicillin content of the aqueous was also higher than that obtained with the other methods tested.

3. The depletion of penicillin from the ocular tissues and the aqueous was almost complete eight hours after iontophoresis with a solution of sodium penicillin containing 5,000 Oxford units of penicillin per cubic centimeter and after application of cotton packs saturated with a solution containing 20,000 Oxford units per cubic centimeter.

4. In general, not more than traces of penicillin were demonstrated in either the lens or the vitreous after topical administration.

5. Determinations on human eyes with normal and with edematous corneas gave more erratic results and much lower values than determinations on rabbits' eyes.

Dr. John H. Dunnington, Dr. Raymond Pfeiffer and Dr. Thomas Johnson permitted the report of their cases.

Miss Jeanette Di Grandi and Miss Mary Glyde Marsh gave technical assistance.

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VITAMIN C SATURATION AND SENILE CATARACT

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Vitamin C ($C_6H_8O_6$) is readily soluble in water and alcohol and insoluble in ether and benzene and has a molecular weight of 176. Fehling's solution is reduced in cold by vitamin C, as is silver nitrate, permanganate and iodide. Von Szent-Györgyi produced vitamin C in 1932 and named it hexuronic acid, without being aware of its true identity. The final identification was made by Tillmans. Vitamin C is characterized by a high redox potential, which is strongly negative. The reduced form of vitamin C activates ferments and inactivates the oxidized form of the same. This vitamin is readily destroyed by oxidation and is a strong reducing agent in itself. Important organs containing ascorbic acid are the adrenals, the lens, the corpus luteum, the brain, the hypophysis, the pancreas, the aqueous and, in lesser amounts, the vitreous. In the blood 8 to 12 mg. per thousand cubic centimeters represents the normal average.

Investigators are unanimous in the opinion that the amount of vitamin C present in the lens and in the aqueous is much higher than in other tissues or in the blood. However, there is a wide discrepancy in the explanations of how this high concentration of vitamin C is produced. This increased amount can be derived either from the blood or through synthesis by the lens. The origin of vitamin C in the lens must still be considered an unsolved problem. It may be that the sugar present in the lens is converted by dehydration into ascorbic acid during glycolysis, with the cystine-cysteine group serving as a hydrogen acceptor, but the conversion might also be due to the reaction of sugar and oxidized glutathione, yielding ascorbic acid and reduced glutathione. It has been proved that in the aging and clouded lens the cysteine group tends to disappear and the cataractous lens is composed of water-soluble and cysteine-free albuminoid. Vitamin C behaves analogously, diminishes as the lens becomes progressively opaque and disappears when the opacification is complete. Since the vitamin C content of the normal aqueous is much higher than that of the blood and since some authors believe this relation is not present in the aphakic eye, the place of origin would seem to be in the lens.

Normal transparency of the lens is linked with normal metabolism. The foundation of the latter is oxidation, the mobilization of hydrogen and the activation of oxygen by help of oxidative ferments. Breathing of the lens is the most important form of oxidation, and in this process the presence of catalyzers, responsible for the oxidation-reduction system, is of paramount significance.

The lens, being devoid of a blood supply, is especially dependent for its normal metabolism on intracellular substances which form oxidation-reduction systems. Birch and Dann [1] were the first to describe the presence of large amounts of vitamin C in the lens of sheep. According to Glick and Biskind,[2] no apparent significance could be attached to the concentration of vitamin C in the lens with regard to the capacity of some animals (such as the rat, rabbit, sheep, ox, cow and horse) to synthesize vitamin C and the lack of this capacity in animals such as the guinea pig and man, who must derive vitamin C from their food. Variations in the concentrations of vitamin C in the lens between these two groups is less than the variations within each group. Thus, the very low value for the rat lens stands in striking contrast to the much higher values for the lenses of other animals of the group capable of synthesizing the vitamin. Müller [3] established high values for the aqueous and the lens of man and animals and considered the possibility that the lens forms vitamin C from sugar. Aging and cataract formation result in diminished sugar and vitamin C contents

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1. Birch, T. W., and Dann, W. J.: Ascorbic Acid in the Eye-Lens and Aqueous Humor of the Ox, Biochem. J. **28**:638, 1934; Estimation and Distribution of Ascorbic Acid and Glutathione in Animal Tissues, Nature, London **131**:469, 1933.

2. Glick, D., and Biskind, G. R.: Studies in Histochemistry: Distribution of Vitamin C in Lens of Eye, Arch. Ophth. **16**:990 (Dec.) 1936.

3. Müller, H. K.: (*a*) Zur Kenntnis der durch Naphthalin hervorgerufenen biochemischen Augenveränderungen und ihre Beeinflussung durch Vitamin C, Arch. f. Augenh. **109**:304, 1935; (*b*) C-Hypovitaminose und Altersstar, Klin. Monatsbl. f. Augenh. **100**:478, 1938.

of the lens; according to Fischer's hypothesis, the production follows the already mentioned formula: sugar + oxidized glutathione = vitamin C + reduced glutathione. The experiments of Guha and Grosh demonstrated the production of vitamin C by enzymatic synthesis through the tissues, especially liver in vitro, and the striking faculty of the lenses of young animals to produce ascorbic acid through synthesis.

The important observation that the vitamin C content of the normal lens diminishes in proportion to the formation of cataract to values approaching zero and, furthermore, that aging of the lens similarly results in decrease of the vitamin C content seems to substantiate the belief that vitamin C is of extreme importance for the respiration of lens tissue. The high vitamin C concentration in the aqueous as compared with that in the blood can be explained on the assumption that the vitamin C content of the aqueous is derived either from the blood or from the lens. Increased intake of vitamin C results in greater excretion in the urine without an increase in the blood level or in the concentration in the aqueous, thus revealing elective filtration rather than ultrafiltration. Von Euler and Malmberg [4] claimed that the antiscorbutic action of the lens is based on the presence of vitamin C, which is much more marked in young animals, thus corroborating the statement that the aging organism and all its structures are poorer in vitamin C and confirming the observation that the amount of the vitamin is lessened in cataractous lenses.

Müller gave the vitamin content of the normal aqueous as 12.8 per hundred cubic centimeters. Nakamura and Nakamura [5] found similarly high concentrations, but for patients with cataractous lenses they obtained a value of 2 to 8 mg. per hundred cubic centimeters and for patients with complicated cataracts, a value of 0.5 mg. per hundred cubic centimeters, thus showing a striking decrease in the aqueous of the aged and of persons with cataract. They observed decreased concentrations in the lens itself, especially in the nucleus. The nucleus has a smaller amount of vitamin C, even in the transparent lens (Glick and Biskind).

Nordmann reported a decrease of ascorbic acid in the cataractous lens to 0.0026 mg. per hundred grams of tissue (the normal was given as from 0.011 to 0.016 mg. per hundred grams). Urbanek [6] derived a change in the vitamin C content of from 1.95 to 14 mg. per hundred cubic centimeters in the aqueous and of from 0.003 to 0.40 mg. per hundred grams in the lens. Hawley and Pearson [7] found a decreased vitamin C content of the cataractous lens and ventured the opinion that the decreased amount of food is responsible for the decrease in the tissues of aging persons and that the decrease within the cataractous lens is only secondary.

A decrease of vitamin C concentration in the aqueous and in the lens of persons with cataract seems to be well established; in the blood the maximum level for such persons is cited as corresponding to the minimum level for normal persons. There is seemingly some connection between the vitamin C level of the blood and the formation of lenticular opacities, a relation which suggests hypovitaminosis C of the lens affected. Hawley and Pearson [7] reported low blood levels in persons with cataract. Bellows [8] found for normal persons 1.02 mg. and for cataractous persons (20 cases) only 0.05 mg., per hundred cubic centimeters; the findings of Urbanek,[6] Gapeev [9] and others represent similarly low values for cataractous patients. According to Bellows, the low level of ascorbic acid in the blood is instrumental in producing the decreased amount in the aqueous, a circumstance predisposing to formation of opacities within the lens. In Müller's opinion, cataract is the result of disturbed metabolism of the lens accompanied with changes in the chemical composition due to decrease of ascorbic acid. Many authors believe that the source of vitamin C in the aqueous lies in the blood; normal aqueous contains the vitamin only in the reduced form and in a concentration not corresponding to that of the blood. According to Goldmann and Buschke,[10] the high concentration of vitamin C in the aqueous is partly the product of the metabolism of the lens. The lens is capable of reducing the oxidized form derived from the blood, a fact partially

4. von Euler, H. V., and Malmberg, M.: Neue Versuche "ueber Askorbinsäure (C-Vitamin) in tierischen Augenlinsen, Arch. f. Augenh. **109**:225, 1935.

5. Nakamura, B., and Nakamura, O.: Ueber das Vitamin C in der Linse und dem Kammerwasser der menschlichen Katarakte, Arch. f. Ophth. **134**:197, 1935.

6. Urbanek, J.: Der C-Vitamin-Stoffwechsel bei Starkranken, Klin. Monatsbl. f. Augenh. **101**:670, 1938. Urbanek, J., and Albrecht, W.: C-Vitamin und Lebensalter, Ztschr. f. Augenh. **95**:192, 1938.

7. Hawley, E., and Pearson, O.: Vitamin C and Its Relation to Cataract, Arch. Ophth. **19**:959, (June) 1938.

8. Bellows, J.: Biochemistry of Lens: Cevitamic Acid Content of the Blood and Urine of Subjects with Senile Cataract, Arch. Ophth. **15**:78 (Jan.) 1936.

9. Gapeev, P. I.: Ascorbic Acid Content of Aqueous Humor, Crystalline Lens and Blood in Cataract Patients and in Normal Persons, Vestnik oftal. **18**:154, 1941.

10. Goldmann, H., and Buschke, W.: Blutkammerwasserschranke und Vitamin C, Arch. f. Augenh. **109**: 205 and 314, 1935; Berichtigung und Nachtrag zu der Arbeit Blutkammerwasserschranke und Vitamin C, ibid. **109**:689, 1936.

explaining the amount of reduced vitamin C in the aqueous; but, as emphasizel by Müller, only a small portion of the vitamin in the aqueous is the product of the lens. The concentration of vitamin C in the aqueous is ten times that in the blood and represents both the oxidized and the reduced phase. Subconjunctival injections of hypertonic saline solution or intravenous injections of theophylline lead to a decrease of ascorbic acid in the aqueous, owing to increased permeability of the blood-aqueous barrier; the complicated cataract due to prolonged inflammation, resulting in decrease in vitamin C concentration, is the clinical analogy to this mechanism. In Buschke's [11] opinion, the vitamin C content of the aqueous depends on the concentration in the blood of the reversible, oxidized, form of vitamin C; the oxidized form in the anterior chamber undergoes reduction through the action of the lens to the reduced phase of the redox system, the lens being the regulating mechanism of the redox potential. Similarly, Monjukowa and Fradkin [12] stated the belief that the vitamin C of the aqueous derives from the blood through the elective function of the ciliary epithelium and unilateral permeability of the blood-aqueous barrier; the change in the latter in cataractous eyes produces the decrease of ascorbic acid. Weinstein's [13] examination disclosed the disappearance of cysteine and vitamin C in cataractous lenses, but in the capsule both were present. In his opinion, the sclerosis of the vessels of aging persons leads to decrease of vitamin C. In the production of the reduced form of vitamin C the lens liberates hydrogen, and this form passes only with difficulty the blood-aqueous barrier. Müller's findings of loss of sugar and increase in ascorbic acid in the lenses of young animals and the reversed condition in older animals seem to be further substantiation of the vitamin C–producing mechanism of the lens. Monjukowa and Fradkin [12] found 20 mg. per hundred grams, in contrast to the concentration in other body tissues. Aging causes decrease; and, in accordance with the slower metabolism of the nucleus, the central portion is poorer than the cortical parts. Müller [3] and his co-workers reported that they had produced naphthalene cataracts in rabbits, and, though there was no change in the concentration of vitamin C in the lenses at first, the values fell to as low as zero as they became cloudier. These cataracts could be prevented by feeding cabbage to the experimental animals, according to Bourne,[14] but Müller and Buschke [15] obtained inconclusive results through treatment of naphthalene cataracts with ascorbic acid. The relatively high concentration of vitamin C in the aqueous was confirmed by Gala and Mělka,[16] who agreed that it must be the result of the lens mechanism, even though their results were lower than the value of 12.8 mg. per hundred cubic centimeters obtained by Müller and Buschke. Tatsumi, Nagao, Okamura and Gamo [17] reported a notable increase of vitamin C in the aqueous after intravenous administration of ascorbic acid (and no change in the level in the spinal fluid), confirming the observation of Goldmann and Buschke [10] of a marked increase in the concentration in the aqueous, lasting several hours, and the similar reports of Bietti [18] and Carteni. The aqueous of aphakic eyes has a much lower concentration of vitamin C (Müller and Buschke), showing that the lens protects vitamin C from oxidation by liberating hydrogen.

In the opinion of some authors, the decreased vitamin C of the aqueous is responsible for the formation of opacities in the lens; however, other investigators, such as Nordmann, Bietti and Carteni, did not accept the decrease as the direct cause of the opacities but regarded it only as a symptom of the metabolic disturbance of the lens.

In a recent paper, Huysmans and Fischer [19] reviewed the various hypotheses offered to explain the increased concentration of vitamin C in the contents of the anterior chamber, the increased activity of the lens (Müller, Fischer), the irreciprocal permeability of the blood–aqueous fluid partition for oxidized vitamin C

11. Buschke, W.: Blutzirkulation im Auge und Vitamin C, Arch. f. Augenh. **109**:691, 1936.

12. Monjukowa, N. K., and Fradkin, M. J.: Neue experimentelle Befunde über die Pathogenese der Katarakt, Arch. f. Ophth. **133**:328, 1935.

13. Weinstein, P.: Bedeutung des C-Vitamins bei den biologischen Oxydationsvorgängen der Linse, Arch. f. Augenh. **109**:221, 1935.

14. Bourne, M. C.: Effect of Diet on Nature of Ocular Lesions Produced by Naphthalene, Brit. J. Ophth. **17**:210, 1933.

15. Müller, H. K., and Buschke, W.: Ueber die Behandlung der Naphthalinkatarakt mit Vitamin C, Arch. f. Augenh. **108**:597, 1934.

16. Gala, A., and Mělka, J.: Der Gehalt an Vitamin C im Humor aqueus des normalen und pathologisch veränderten Auges, Arch. f. Augenh. **109**:726, 1936.

17. Tatsumi, M.; Nagao, Y.; Okamura, K., and Gamo, J.: Ueber den Uebergang von Vitamin C in den Liquor und das Augenkammerwasser, Klin. Wchnschr. **14**:1007, 1935.

18. Bietti, G. B.: Ulteriori ricerche intorno all'azione sul cristallino di regimi carenzati di vitamina e di cistina, Boll. d'ocul. **14**:3, 1935.

19. Huysmans, J. H. B. M., and Fischer, F. P.: Ueber die Ursachen der hohen Vitamin-C-Konzentration von Kammerwasser und Linse, Ophthalmologica **103**:21, 1942.

(Goldmann and Buschke [19]), the combined origin from the blood and lens (Podesta and Baucke [20]) and the stimulation of the epithelium through the parasympathetic system (Bonsignore).

According to Müller, the oxidized form of vitamin C appears in the aqueous through diffusion from the blood and becomes changed into the reduced form through activity of the lens. Fischer's concept of the production of vitamin C from carbohydrates through the metabolism of the lens, as mentioned before, represents a reversible oxidation-reduction system: 1 molecule of dextrose combining with 2 molecules of oxidized glutathione, resulting in 1 molecule of vitamin C and 4 molecules of reduced glutathione. Goldmann and Buschke stated the opinion that vitamin C exists in the blood in oxidized form, subconjunctival injections of saline solution and intravenous administration of theophylline resulting in lessening of the amount present in the aqueous and injection of epinephrine not causing any increase in the concentration in the aqueous. Injection of vitamin C resulted, after half an hour, in the absence of the reduced form of vitamin C in the blood and a slight increase of the oxidized form but in a long-lasting increase in the concentration of the aqueous. Increased concentration in the blood was accompanied with increased concentration in the anterior chamber. According to Fischer, vitamin C in the blood almost always exists as the reduced form, and the decreased concentration following injection of epinephrine is due to oxidation of vitamin C and not to rendering impermeable the blood–aqueous partition; accordingly, substitution of epinephrine by atropine produces an increased concentration of vitamin C in the aqueous. Furthermore, the concentration of vitamin C in the aqueous of the aphakic eye approaches that of the blood; in certain types of secondary cataract the presence of newly formed lens tissue is responsible for the increased amount of ascorbic acid present.

The lens not only produces vitamin C but reduces large quantities of the oxidized form. The concentrations of vitamin C in the lens and aqueous regulate the transparency of the lens; the concentration may be normal in lenses with nuclear sclerosis with functioning clear cortical parts. The circulation of the aqueous toward and the return circulation from the lens and the circulation within the lens itself are the factors representing the reduction of vitamin C.

20. Podesta, H., and Baucke, J.: Woher kommt das Vitamin C in den verschiedenen Geweben des Auges? Herkunft aus dem Blute und Synthese in der Linse, Arch. f. Ophth. **139**:720, 1938.

The hypothesis of Fischer concerning the concentration of the vitamin in the aqueous of aphakic eyes is seemingly contradicted by many authors. Urbanek reported a wide variation of the concentration in aphakic eyes, which apparently is in contradiction to the concept that the lens is responsible either for the amount or for the production of vitamin C in the aqueous. Franta [21] found that the aqueous of young aphakic persons years after the operation contains various amounts of vitamin C, values which approach the level for eyes without aphakia. For an 11 year old child, nine years after the operation, the concentrations for the two eyes were 14.80 and 11.28 mg. per hundred cubic centimeters, respectively; for a 7 year old child, two years after the operation, the value was 6.52 mg., and, finally, for a 5 year old child, six months after the operation, the concentrations were 3.52 and 4.23 mg. per hundred cubic centimeters. Bakker,[22] on the other hand, reported decreased concentrations in cases of aphakia. The possible role of vitamin C in the metabolism of the lens and the relation of its disturbance to formation of cataract led the investigations in the direction of a systemic disturbance of the vitamin C metabolism in patients with senile cataract. It is clear that the patients with cataract do not show clinical symptoms of hypovitaminosis C. Mild deficiency may cause weakness, headache, restlessness, tenderness of the joints, retarded growth, impaired digestion, defective teeth, lowered resistance to infection and slow union of fractures. Pronounced deficiency may cause scurvy, characterized by capillary hemorrhages, epistaxis, swollen joints, gingivitis, loosened teeth, spontaneous fractures, anemia, muscle atrophy, infections of the respiratory and intestinal tracts, bloody diarrhea and hematuria, with death due to secondary infection or shock. Bakker emphasized that there are cases of complete lack of vitamin C in which the lenses are transparent. Scurvy is known never to cause cataract formation, nor does it occur in experimental animals in which the lens and aqueous have been depleted of vitamin C. In the experiments of Monjukowa and Fradkin it was produced only in the extreme stages, in which numerous factors besides the depletion of vitamin C could be blamed. This fact did not escape the attention of Williamson-Noble,[23]

21. Franta, J.: L'acide ascorbique dans l'humeur aqueuse, Compt. rend. Soc. de biol. **126**:110, 1937.

22. Bakker, A.: Ueber die Bedeutung der Askorbinsäure (Vitamin C) für den Stoffwechsel der Linse, Arch. f. Ophth. **136**:166, 1936.

(Footnotes continued on next page)

but, in his opinion, it may be that ascorbic acid provides a method of lens respiration which serves as an alternative to that given by glutathione. When the latter mechanism is upset, as in the case of naphthalene or galactose cataract, vitamin C comes into its own; in fact, administration of the latter substance has been shown to delay the onset of galactose cataract, though not to the same extent as the use of cysteine, the amino acid–forming glutathione.

Research on the true role of vitamin C in cataract formation had to be extended, and studies concerned with the clinical and laboratory examinations of cataractous patients formed the next logical step in clearing up the question.

In normal, healthy persons the blood serum or plasma level and the urinary excretion of vitamin C are dependent on the dietary intake and the utilization of food. Normal adults, according to van Eekelen [24] and Heinemann,[25] have a daily requirement of the vitamin of 60 mg. The presence of infection is known to increase the requirement; the blood level of vitamin C in patients with infection may be reduced to the level found in patients with scurvy, and the amount of vitamin required to raise the blood plasma level to the value for the renal threshold and to maintain this degree of saturation is many times that accepted as a normal physiologic requirement. Similarly, patients with rheumatoid arthritis exhibit an apparent vitamin C deficiency.

By saturation is meant a state of supply of ascorbic acid such that after an increased intake 60 to 80 per cent of the additional vitamin will be excreted in the urine within eight to twenty-four hours. Hence, unsaturation exists when only a slight increase in excretion follows the added intake. This does not indicate that undersaturation is an abnormal state or that a supply inadequate to provide saturation will cause vitamin C deficiency. The majority of persons who do not show any detectable signs of deficiency are not saturated. The normal plasma level of 1.2 mg. per hundred cubic centimeters falls in cases of scurvy to 0.2 mg. per hundred cubic centimeters, but abnormally low levels are encountered without evidence of deficiency. The urinary excretion normally varies from 10 to 30 mg. daily. The amount varies not only with the method of analysis but with the protein content and the acid-base properties of the diet. Excretions above 15 mg. of vitamin C daily suggest the absence of any deficiency, but persons excreting that amount may be saturated or may be very far from saturation. The requirements of aging bring with it the necessity for a larger amount of vitamin C. This statement seems to contradict the well known fact that advancing age requires less nutrition; on the other hand, the progressive atrophy of the organs makes the utilization of food more difficult. The absorption of dextrose in the intestine requires vitamin C. Therefore in the aged a higher requirement of vitamin C is probable for the proper upkeep of nutritional balance. Furthermore, in senescence the saturation suffers, owing to poorer absorption, facilitated by the often present suboptimal secretion of hydrochloric acid in the stomach and unsatisfactory mastication. All these circumstances may be instrumental in producing comparatively lower plasma levels, a decrease which is not necessarily indicative of vitamin deficiency. The plasma and blood levels and the urinary excretion do not give as accurate information concerning vitamin C nutrition as the saturation test—the measuring of urinary output following an added intake of the vitamin. Oral administration gives less accurate information than the intravenous method; with the former there are large factors of error due to variability of absorption and utilization from the gastrointestinal tract. Wright, Lilienfeld and MacLenathen [26] proposed a five hour test following intravenous injection. In our examinations the method of Finkle [27] was followed.

On the day of the test the patient was permitted the usual meals, with the exception of citrus fruit and other foods rich in vitamin C. There was no restriction of fluids. The urine was collected at 8 a. m. and at 10 a. m. and the vitamin C content determined for each specimen. After the 10 a. m. voiding 100 mg. of ascorbic acid, dissolved in 5 cc. of distilled water, was administered intravenously. The subject was requested to void at 12:30, 2:30 and 4:30 p. m., and the vitamin C content of each specimen was again determined. For the titration of ascorbic acid, 2,6-dichlorophenolindophenol, as used by Harris, Ray and Ward,[28] was employed. The injection in 220 aged subjects did not result in any untoward symptoms.

23. Williamson-Noble, F. A.: Discussion of Role of Vitamins in Ophthalmology, Tr. Ophth. Soc. U. Kingdom (1942) **62**:53, 1943.

24. van Eekelen, M.: On the Amount of Ascorbic Acid in the Blood and Urine: Daily Human Requirements for Ascorbic Acid, Biochem. J. **30**:2291, 1936.

25. Heinemann, M.: On the Relation Between Diet and Urinary Output of Thiosulfate and Ascorbic Acid: Human Requirements for Vitamin C, Biochem. J. **30**: 2299, 1936.

26. Wright, I. S.; Lilienfeld, A., and MacLenathen, E.: Determination of Vitamin C Saturation: Five Hour Test After Intravenous Test Dose, Arch. Int. Med. **60**:264 (Aug.) 1937.

27. Finkle, P.: Vitamin C Saturation Levels in the Body in Normal Subjects and in Various Pathological Conditions, J. Clin. Investigation **16**:587, 1937.

28. Harris, L. J.; Ray, S. N., and Ward, A.: The Excretion of Vitamin C in Human Urine and Its Dependence on the Dietary Intake, Biochem. J. **27**:2011, 1933.

In the unselected series were included 200 patients with senile cataract, the ages varying from 50 to 84, and 20 patients with glaucoma without cataract, representing approximately the same age group. All patients were admitted for the purpose of surgical intervention, and the tests were made on the first day of hospitalization. Patients who refused the intravenous administration or did not cooperate in observation of the voiding time were necessarily excluded from the study.

The vitamin C output within twenty-four hours was usually about 13 to 20 mg., and the average excretion was between 0.03 and 0.05 mg. per cubic centimeter of urine during the day and a somewhat lower amount during the night. The intravenous injection in normal subjects produces an increased excretion of about six times the preinjection amount; this means that, in addition to the usual daily excretion, 30 to 50 per cent (or more) of the injected amount is eliminated through the kidneys. For determination of the vitamin C saturation of the body, measurement of the excretion for eight hours, including the six hours following the injection, suffices. This procedure is highly satisfactory except in cases of impairment of renal function, in which delay in excretion may occur (Ludden and Wright [29]).

Of the 20 control subjects, 12 showed after the intravenous injection an excretion of from four to eight times the previous amount, and 5 patients, an excretion of from two to four times the preinjection value; in the remaining 3 subjects the urinary excretion was less than twice the preinjection value.

The distribution of values for the 200 unselected patients with cataract was as follows:

1. In 10 patients the excretion of vitamin C was increased to from six to eight times the amount preceding intravenous administration of ascorbic acid.

2. In 125 patients the urinary output was four to six times that established before the administration of ascorbic acid.

3. In 37 patients the output averaged only two to four times the preinjection value.

4. The remaining 33 patients showed less than twice the amount of vitamin C excreted before administration of the ascorbic acid.

When the ages of the patients are considered in relation to the vitamin C excretion in the urine, it is evident that the majority of the patients with a high vitamin C excretion belonged to the lower age group (50 to 60 years) and, conversely, that the majority of the group with poor vitamin C saturation belonged to the higher age group (60 to 70 years and over 70 years).

The great majority of my patients (135) showed an excretion level approximating that found in the normal subjects living on an adequate mixed diet; a large percentage were within the age group of 50 to 60 years. In the older group were subjects whose excretion level of vitamin C was considerably lower (37 patients, two to four times, and 33 patients less than twice, the preinjection value), thus indicating subnormal saturation levels; the patients of this group were more of the senescent type, some of them being well over 70 and some 80 years of age, a period at which the possibility of renal impairment of excretion, with or without the symptoms of renal insufficiency, must be considered.

The literature often contains data on vitamin C deficiency in connection with the formation of cataract, postoperative bleeding or retinal hemorrhages and authors even recommend therapeutic measures based on these findings. The deficiency was often established on plasma or blood levels or on the urinary excretion; in my experience, however, only the saturation test furnishes a quantitative index of the level of vitamin C nutrition. It must be regarded as erroneous to draw conclusions merely from a single determination of the vitamin C content of the urine. The saturation test disclosed, first, that there is no deviation in hemorrhagic diathesis, such as Werlhof's disease (thrombopenic purpura), Henoch-Schönlein purpura and hemophilia; only in some cases of so-called essential thrombopenic purpura is C avitaminosis the etiologic factor.

The so-called intradermal test (Rotter, Portney and Wilkinson; Reddy and Sastry [30]), based on the intradermal injection of 2,6-dichlorophenolindophenol and the decoloration of the wheal produced under action of the ingested vitamin C, seems a less accurate method of determination than the saturation test.

Seefried [31] employed the saturation test with a small number of cataractous patients, administering 300 mg. of ascorbic acid orally daily until the urine contained 150 mg. of the vitamin. The cataractous patients needed a longer period of administration than the normal con-

29. Ludden, J. B., and Wright, I.: Effect of Renal Retention of Vitamin C on Saturation Tests: Formula for Compensation of This Factor of Error, Arch. Int. Med. **65**:151 (Jan.) 1940.

30. Reddy, D. V. S., and Sastry, P. B.: Intradermal Test for Vitamin C Nutrition of Body in Ophthalmic Patients, J. Indian M. A. **10**:440, 1941.

31. Seefried, J.: Ueber den Vitamin C-Haushalt der Alterstarkranken, Arch. f. Ophth. **138**:620, 1938.

trols of the same age. He concluded that patients with senile cataract require for saturation a greater intake of vitamin C than control patients, the disturbance of the vitamin C metabolism of the entire body exerting a favorable influence for development of the opacities in the lens. Karbacher,[32] of Vogt's clinic, found no significant difference in saturability with vitamin C between patients with cataracts and normal controls of the same age, and he therefore expressed doubt of the presence of a systemic disturbance of vitamin C metabolism in patients with senile cataract. Urbanek employed the saturation test and measured the urinary excretion and the blood level of vitamin C; he found a higher excretion in the urine in the young than in the aged, in spite of the activity of the former. The saturation level of the aged proved to be the same whether or not cataract was present, more vitamin C being necessary to reach saturation irrespective of the presence of cataract; the apparent diet is a more important factor, vegetarians showing a lower degree of saturation. Gapeev arrived at a similar conclusion, namely, that the large amount of vitamin C in the aqueous and in the lens as compared with the low level in the blood of patients with cataract does not indicate any relationship. The aqueous of normal eyes showed 7.7 to 15 mg. of vitamin C per hundred cubic centimeters; the lens, 7.8 to 15.8 mg. per hundred grams; the aqueous of cataractous eyes, from 2.9 to 7.4 mg.; the lens extracted by the intracapsular method, 2.8 to 7.2 mg., and the lens extracted by the extracapsular method, 1.35 to 5.2 mg. per hundred grams. The blood values for normal subjects were 0.3 to 1.2 mg., and those for patients with cataract, 0.8 to 0.46 mg. per hundred cubic centimeters.

The human body is unable to synthesize vitamin C, as some animals can, and therefore depends entirely on an extraneous supply. Patients with some form of chronic illness, such as peptic ulcer, gallbladder disease and obstructive gastrointestinal lesions, and often aged people with poor dentition and mastication, confine their diet to soft, well cooked foods, which are almost totally lacking in vitamin C. Their diets are especially deficient in orange juice, fresh fruits and raw vegetables, the chief source of vitamin C. The average mixed diet maintains a normal vitamin C level, with little tissue reserve and a low urinary output. Depletion of vitamin C results either from an unbalanced diet (lower intake) or from a disturbance of utilization; in the aged both possibilities must be considered; these persons may show a low blood level or a low urinary excretion of vitamin C which is not indicative of hypovitaminosis. The saturation test, the measurement of the characteristic rise in excretion of vitamin C following intravenous administration of ascorbic acid, is the test indicative of a definite saturation level. In the case of patients responding with the typical increased excretion after intravenous administration of ascorbic acid, it may be assumed that the body is definitely at the saturation level. Only the group in which administration is not followed by an increase in urinary output within the next five or six hours can be considered as having a level of saturation below the normal, and therefore as belonging to the group with vitamin C deficiency. Undersaturation is present in a considerable proportion of the population and is often misinterpreted as the basis of various pathologic conditions. In my unselected series of patients the majority did not present any clinical deficiency of vitamin C; this is hardly understandable if hypovitaminosis C of the body is to be considered the underlying cause of the formation of opacities in the lens. In the smaller group the saturation test showed a degree of vitamin C deficiency which is often present with purpura and various pathologic conditions, without having any significance, undoubtedly being merely part of the general dietary deficiency. The more frequent occurrence of this deficiency in the higher age group speaks, rather, for the deficiency characteristic of senescence, and not for any causal relationship to cataract formation. In spite of all the work done with vitamin C depletion of the body, there is no conclusive proof that vitamin C deficiency is the cause of any disease other than scurvy. A dietary intake inherently poor in this substance or the presence of a disease with higher requirements of the vitamins, such as febrile conditions, hyperthyroidism, malignant growths and leukemia, is accompanied with vitamin C deficiency. The vitamin C deficiency of some of the cataractous patients is a sequel to poor intake, poorer utilization and possible lower elimination of vitamin C by the kidneys and is characteristic of geriatric shortcomings.

Vogt[33] expressed himself as against the hypothesis that hypovitaminosis C is the cause of cataract; the hypovitaminosis is part of senescence, which only parallels and is coordinated with the formation of cataract. On the

32. Karbacher, P.: Kritische Bemerkungen zu Johannes Seefrieds Arbeit: Ueber den Vitamin C-Haushalt der "Altersstarkranken," Arch. f. Ophth. **140**: 748, 1939.

33. Vogt, A.: Zur Stardiskussion in Heidelberg, Klin. Monatsbl. f. Augenh. **101**:530, 1938.

basis of observations on aged identical twins, Vogt[34] concluded that senile cataract develops irretrievably and inevitably from the genetic anlage. In the same way in which the germ plasma is responsible for the life span of the organism (inheritance of longevity), it is the determining factor in the aging of the single organ. Accordingly, the senile cataract is similar to the forms of cataract representing genotypical or idiokinetic pathologic processes in the lens, and the differences of cataract formation in identical twins are quantitative but not qualitative. Von Szily[35] stated the belief that the assumption of absolute morphologic and genetic identity is unjustified. If senile cataract represents senile involution and premature dying of the lens, the premature senility, like altered basal metabolism, depends not only on genes but on secretion of the gonads, the thyroid, the pituitary and the adrenal glands, which influence and determine the individual type of aging. Vogt's contention that the senile cataract represents only the expression of heredity, and that therefore chemical studies must be futile, brought further objections from Krause,[36] who mentioned the amenability of hereditary diseases to therapy, for example, the treatment of diabetes with insulin and the use of thyroxine for hypothyroidism of identical twins. This discussion, the by-product of research on vitamin C as the causative factor in cataract, leads into the realm of genetics. One of the most common misconceptions of genetic laws seems to be the conclusion that if a character is conditioned by heredity it cannot be modified by environment. Hence, even if the concept of the hereditary basis of senile cataract were to be accepted, it would not exclude the possibility of environmental influences, of which metabolism, directly or indirectly (as vitamin C influencing the adrenal cortex), is only one of the numerous factors.

34. Vogt, A.: Weitere Augenstudien an eineiigen Zwillingen höheren Alters über die Vererbung der Altersmerkmale, Klin. Monatsbl. f. Augenh. **100**:497, 1938.

35. Von Szily, A.: Newer Aspects of Affections of the Lens, in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, New York, Paul B. Hoeber, Inc., 1940, p. 436.

36. Krause, A. C.: Medical Treatment of Senile Cataract, Arch. Ophth. **23**:487 (March) 1940.

SUMMARY

The saturation test, the measurement of vitamin C output after intravenous injection of ascorbic acid, is the most accurate index of vitamin C deficiency.

Of 200 unselected patients with cataract, 135 (62.5 per cent) revealed a saturation level of the body for vitamin C.

The rest of the series, 65 patients, showed a low level of vitamin C excretion after intravenous administration of ascorbic acid. In 35 patients (18.5 per cent) the deficiency was mild, and in 33 patients (16.5 per cent) it was more pronounced, representing a general deficiency.

There is not sufficient evidence to indicate that vitamin C deficiency contributes to the formation of cataract. Transparency of the lens is not dependent on the vitamin C saturation of the body, since the large number of senile cataracts associated with a normal saturation level would contradict such an assumption.

The vitamin C deficiency of some of the cataractous patients seems to be the natural result of the vitamin C deficiency of old age.

31 Lincoln Park.

SYMMETRIC DEFECTS IN THE LOWER LIDS ASSOCIATED WITH ABNORMALITIES OF THE ZYGOMATIC PROCESSES OF THE TEMPORAL BONES

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PHILADELPHIA

In 1888 Berry [1] described symmetric notches in the outer portion of the lower lids in a mother whose daughter had a similar defect in one lower eyelid. Although Berry did not examine the mother's brother, the latter reputedly had a similar defect in one eye. The affected child's brother had no ocular defect but a harelip, and her older sister showed no clinical defects.

Fig. 1.—*A*, defects of the outer third of each lower lid in a 3 year old Negro girl. *B*, a close-up of the right eye of the same patient.

In 1900 Treacher Collins [2] recorded 2 cases of symmetric congenital notching in the outer part of each lower lid associated with clinical evidence of defective development of the malar bones. The family history was negative for the condition in 1 case and was not mentioned in the other.

In 1927 Isakowitz [3] described a similar case of symmetric notching of the outer portion of each lower lid. He stated the opinion that these defects were probably colobomas. Although he did not examine the father and sister of the patient reported on, studies of photographs indicated that they possessed the same symmetric defects of the lower lids. Isakowitz,[3] apparently unaware of the previous observations of Collins,[2] noted a depression of the orbital rim and suggested that a defect might exist in the zygoma. He did not examine his patient roentgenographically.

In 1932 Waardenburg [4] mentioned a single similar case that he had observed but did not discuss any associated findings or the family history.

In 1943 2 similar cases were reported by Mann and Kilner [5] and another by Johnstone.[6] Mann could find no ocular defects other than the involvement of the eyelid in the case which she reported, but she did present roentgenographic evidence of defective development of all the facial bones. The malar bones were very small and structurally malformed. Embryologically, Mann considers this type of case as one of retardation of differentiation of the maxillary mesoderm at and after the 50 mm. stage. Kilner's [5] case was similar to that reported by Mann. However, his case history was more complete. As reported by Kilner, the affected child had a sister without any abnormality, and no family history of congenital defects was

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From the Departments of Ophthalmology, Radiology and Social Service of the Hospital of the University of Pennsylvania.

1. Berry, G. A.: Note on a Congenital Defect (? Coloboma) of the Lower Lid, Roy. London Ophth. Hosp. Rep. **12**:255, 1888.

2. Collins, T.: Symmetrical Congenital Notches in Outer Part of Each Lower Lid and Defective Development of the Malar Bones, Tr. Ophth. Soc. U. Kingdom **20**:90, 1900.

3. Isakowitz, J.: Eine seltene erbliche Anomalie der Lidspalte (atypisches Lidkolobom?), Klin Montasbl. f. Augenh. **78**:509, 1927.

4. Waardenburg, P. J.: Das menschliche Auge und seine Erbanlagen, Haag, Martinius Nijhoff, 1932, pp. 50-51.

5. Mann, I., and Kilner, T. P.: Deficiency of Malar Bones with Defect of Lower Lids, Brit. J. Ophth. **27**:13, 1943.

6. Johnstone, I. L.: Deficiency of Malar Bones with Defect of Lower Lids, Brit. J. Ophth. **27**:21, 1943.

elicited. Kilner's patient also had a harelip. No roentgenographic study was mentioned.

Johnstone's [6] case was similar, and roentgenographic changes showing poor development of the zygomas were noted.

Of these several papers, only Berry's [1] and Isakowitz' [3] suggest the hereditary nature of this lesion. The case reports of Mann [5] and Johnstone [6] include no family history. One of Collins' [2] cases, as well as Kilner's [5] case, as

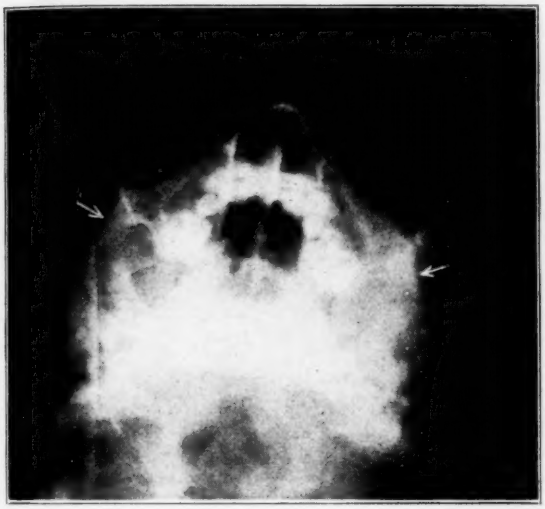

Fig. 2.—Roentgenogram of a skull of 3 year old Negro girl, showing defects of the zygomatic processes of the temporal bones. Compare with the normal processes shown in figure 5.

recorded, appeared to be isolated instances in families with negative histories. Berry's [1] cases are not exactly similar to those observed later. His were the only cases in which the defect was unilateral, and he was unable to exclude the possibility of ocular trauma in the case of the mother's brother. He did not mention any abnormality of the facial bones.

In not one of the aforementioned reports was roentgenographic evidence of deficiencies of the zygomas sought for in other members of families of patients showing this symmetric defect of the lower lid. Such a malformation, if present, would be informative evidence of the hereditary nature of this defect.

REPORT OF A CASE

A similar case was recently observed in the ophthalmologic department of the Hospital of the University of Pennsylvania. V. S., a 3 year old Negro girl, suffering from lead poisoning, was referred to the ophthalmologic service by the pediatric department. External examination revealed the marked deformity of both lower lids. The deformities were symmetric and involved the outer portion of each lower lid (fig. 1). The underlying cheek appeared depressed on each side. The upper lids were drawn down slightly at the outer canthi. The inner portion of each lower lid showed no lashes or meibomian glands (this defect was noted in the cases of Isakowitz and Mann). No other ocular abnormalities could be noted on external, biomicroscopic or ophthalmoscopic examinations. No deformities of the ears, lips or palate were observed, but the upper jaw appeared to be narrowed. In addition to suffering from lead poisoning, the child presented a behavior problem and was extremely uncooperative. Her obstreperous nature did not lend itself to roentgenographic study, and only after three attempts could satisfactory exposures be obtained. These roentgenograms revealed a defect of the zygomatic processes of the temporal bones (fig. 2).

The roentgenologic report on the patient was as follows: The zygomatic processes of the temporal bones were absent bilaterally. There was no disporportion between the bones of the vault and those of the face and the base of the skull. The fontanels were closed, but there was a persistent frontal suture. The bones of the face were well developed, and the maxillary sinuses were large. The maxillary teeth were well developed and showed no malocclusion with the mandibular teeth. The zygomatic bones were normal.

The clavicles and the long bones showed no abnormality at this time. In the fall of 1944 the long bones showed evidence of lead lines in the metaphyses.

The ocular findings in this case resembled strikingly those reported by Collins,[2] Isakowitz,[3] Waardenburg,[4] Mann [5] (first case) and Johnstone.[6]

The mother and the maternal grandfather of the child displayed similar symmetric defects of the lower

Fig. 3.—*A*, symmetric defects in the outer third of each lower lid in the mother of the child shown in figure 1. *B*, symmetric defects in the outer third of each lower lid of the grandfather of the same child. The defect has been altered by angular tarsorrhaphies, performed many years ago.

lids, with depression of the underlying portion of each cheek. The changes in the mother's lids were definite but not as pronounced as the child's. The grandfather's were evident but, again, were not as marked as the grandchild's. Angular tarsorrhaphies had been performed many years previously (fig. 3 *A* and *B*). No disturbances of the lashes or of the meibomian glands were noted in the grandfather, but some reduction in the number of cilia and thinning of the lid existed in the

mother. Both the mother and the grandfather had visual acuity in each eye of 6/6 without correction. No other ocular defect could be found in either. No deformities of the ears, lips or palate were present. Roentgenographic studies revealed bilateral absence of the zygomatic processes in both the mother and the grandfather (fig. 4).

The roentgenographic reports on the mother and the grandfather were as follows:

S. S., aged 50, a Negro, had bilateral absence of the zygomatic processes of the temporal bones. The contours of the skull were not abnormal in that there appeared to be no disproportion between the bones of the vault and the bones of the face and the base of the skull. The maxilla was normal, and the maxillary sinuses were well developed. The tips of the zygomatic bones forming the anterior portion of the zygomatic arch may have been shorter than one normally sees.

V. S., aged 30, a Negro woman, had bilateral absence of the zygomatic processes of the temporal bones. The bones of the vault appeared slightly larger than the bones of the base of the skull and of the face. The maxilla was well developed, with good-sized maxillary sinuses, and the maxillary teeth were well formed, with no evidence of malocclusion with the mandibular teeth. The zygomatic bones were well developed. The clavicles showed no abnormality of development.

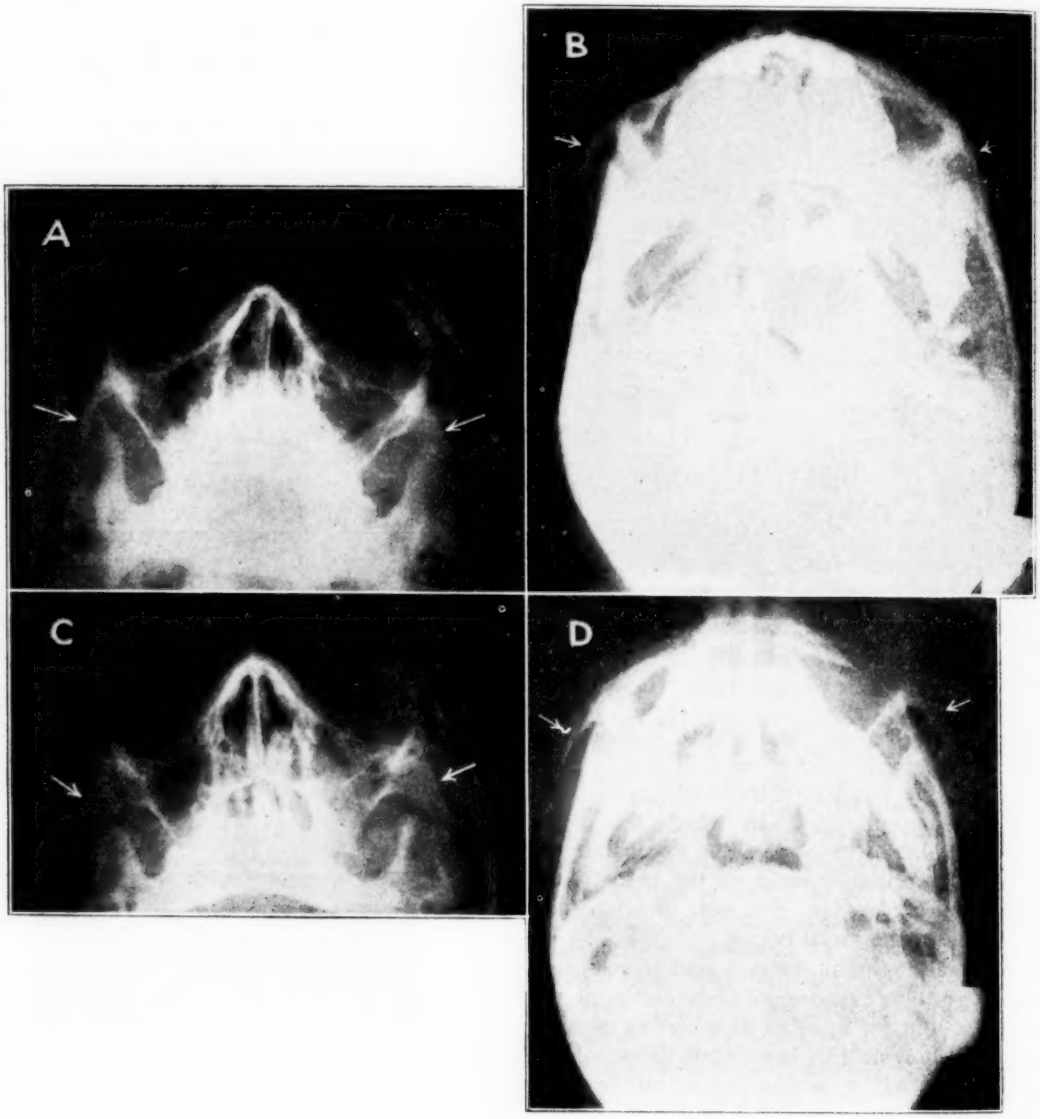

Fig. 4.—Two views of the head of the mother (*A* and *B*) and of the grandfather (*C* and *D*), showing bilateral absence of the zygomatic processes of the temporal bones. In one view of the mother (*B*) the head is turned so that only one process can be clearly seen.

Careful inquiry, with the study of family photographs, revealed an interesting pedigree based on the abnormality of the lids (fig. 6). The shaded figures in the chart represent members of the family with probable involvement, according to the information supplied by the mother and the grandfather, but for whom evidence was questionable because of lack of satisfactory photo-

graphs. The black symbols indicate members who were definitely affected as evidenced by the history and by photographs. All of the surviving members of the family are spread over the United States and either could not be reached or could not be induced to undergo an ophthalmologic or a roentgenologic study. It is possible that the child's uncle, who fails to demonstrate any significant defect of the lids, may possess deficient zygomatic processes.

The condition presented by this family is unquestionably a hereditary dysostosis but not a manifestation of the more common cleidocranial dysostosis. Fitzwilliams [7] said of the facial contour of the 40 patients with cleidocranial dysostosis whom he examined:

> In every case where the skull changes are present . . . they are accompanied by profound alteration in the skeleton of the face. . . . The face itself [is] frequently described as small, and small it is when compared with the normal. The disparity in size between the small face and large head is frequently well depicted in illustrations which accompany many of the published records of this condition. . . . The supra-orbital ridges . . . partaking in the increased girth of the cranium, prominently overhang the orbits, while the bones bounding the orbits below, in common with the majority of bones of the face, are small and ill-developed and appear flattened or sunken in comparison. The roof of the orbit is sometimes depressed, thus causing some degree of exophthalmos. The general aspect of the orbit resembles that of a patient with a mild degree of hydrocephaly.

Stocks,[8] in an analysis of 136 cases of cleidocranial dysostosis, stated that there were normal clavicles in only 2 instances. In none of these cases were defects in the zygomatic processes of the temporal bones reported.

In the case reported by Mann [5] considerable changes were shown in the facial bones, as well as in the sternum. The clavicles were not specifically mentioned. It is not possible, from the evidence presented, to exclude her case from the cleidocranial dysostosis group. The case of Kilner [5] may also be of this type. Stocks' [8] statistics reveal that in 55 per cent of the cases of cleidocranial dysostosis there were abnormalities of the palate. Kilner's [5] patient had a cleft palate. Unfortunately, roentgenographic examinations of the clavicles and of the facial bones were not included in the report.

In the reports by Berry,[1] Collins [2] Isakowitz [3] and Waardenburg [4] the data were not sufficient to allow one to exclude their cases from the group with cleidocranial dysostosis.

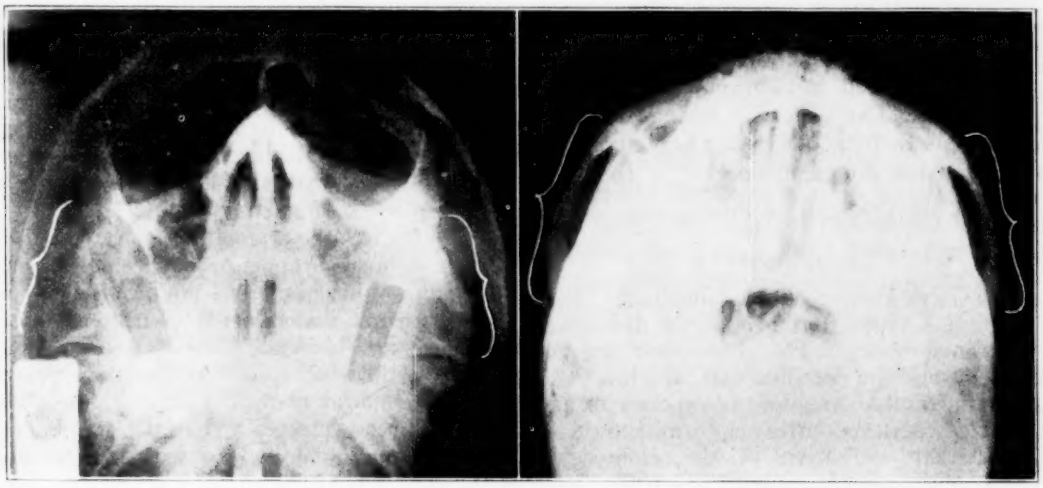

Fig. 5.—Two views of normal zygomatic processes.

Fig. 6.—Pedigree of symmetric defects of the outer portions of the lower lids associated with bilateral absence of the zygomatic processes of the temporal bones. *1* indicates the child; *2*, the mother, and *3*, the grandparent, whose cases are described in the text.

The unshaded figures indicate that the lids were not involved; the black figures, that there was definite evidence of involvement of the lids, and the shaded figures, that the evidence was questionably positive (uncertain history and no photographs).

7. Fitzwilliams, D. C. L.: Hereditary Cranio-cleidodysostosis, Lancet **2**:1466-1475, 1910.

8. Stocks, P., in Pearson, K.: The Treasury of Human Inheritance: III. Hereditary Disorders of Bone Development, Eugenics Laboratory Memoirs 22, London, Cambridge University Press, 1925.

The pedigree in the present cases suggests that the responsible gene is a dominant one. Roentgenographic studies have established the fact that the deficiency of the zygomatic process is associated with the deformity of the lower lid and, in addition, have demonstrated that the osseous deficiency is similarly transmitted. The presence of normal facial bones, other than the zygomatic process of the temporal bone, and of normal clavicles would exclude these cases from the cleidocranial dysostosis group.

Although the defects of the lids in the 3 cases presented here are similar to those observed by Collins,[2] Isakowitz,[3] Mann and Kilner[5] and Johnstone,[6] the bony defects are chiefly of the zygomatic processes of the temporal bones, and not of the zygomas, as described in the other reports.

SUMMARY

Symmetric defects in the outer third of each lower lid, with absence of the zygomatic processes of the temporal bones, as shown roentgenographically, occurred in a grandparent, mother and daughter. The ancestral history of these cases suggests that the defect was hereditary and that the trait is a dominant one.

Hospital of the University of Pennsylvania.

DISCUSSION

DR. FRANCIS MAHONEY, Philadelphia: There are numerous types and groups of dysostoses of the cranial bones. The commonest are the meningocele and the encephalocele, and less common is congenital absence of the superior orbital wall. In cases of the latter malformity there is a characteristic pulsation of the globe synchronous with cardiac pulsations. The least common type of cranial dysostosis is *Lüchenschädel,* or the lacework skull. This is the most severe and extensive of the dysostoses of the skull. None of these forms is hereditary.

Three types with a hereditary link have been reported. The defect represented by our cases is, I believe, the fourth type in this series. The most spectacular of these types, of course, is the hereditary cleidocranial dysostosis, in which cranial defects are associated with deficiency or absence of the clavicles. Some persons with this defect can bend forward and touch their shoulders together. They have, as Dr. Leopold has described, changes in the facial bones, but these changes are in the maxilla, with deficiencies in the maxillary teeth and malocclusion with the mandibular teeth.

Another type is the hereditary craniofacial dysostosis. In this type changes in the skull and facial bones appear to be similar to those associated with cleidocranial dysostosis without the abnormalities of the clavicles.

The third type, which seems most closely related to the defect in our cases, is represented by the hereditary ectodermal dysplasias. In this condition there is a deficiency in the sweat glands and scanty or missing hair. Usually the upper incisor teeth are absent. The skull has the appearance of hydrocephaly, with a "too large head on a too small face."

In our cases the cranial bones are well formed. There is no disproportion between the bones of the vault and the bones of the face. There is no deficiency or malocclusion of the teeth. The clavicles are normal. The only osseous deficiency is the absence of the zygomatic processes of the temporal bones. However, the changes in the lower eyelashes and in the glands around them point to some link with the hereditary ectodermal dysplasias.

VALUE OF CULTURES BEFORE OPERATION FOR CATARACT

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A study of a series of 2,508 operations for cataract extraction was made to determine the value of preoperative cultures in the prognosis of postoperative infections and the influence of chemotherapy.

For the past eight years cultures of the eyes of patients admitted for cataract extraction have been examined for their bacterial flora. The purpose of this study was to determine whether any particular micro-organisms were responsible for postoperative infections. More recently these bacteriologic studies have been extended to aid in the evaluation of preoperative prophylactic chemotherapy.

PROCEDURES FOR PREOPERATIVE CULTURES

In the cases reported the following uniform method was carried out: The patient was admitted a day prior to the cataract operation, and cultures of material from both eyes were made as follows:[1] Sterile cotton swabs, moistened in 1 per cent dextrose infusion broth were rubbed firmly twice (back and forth) over the greater part of the lower conjunctiva, carefully avoiding the lid border and the lashes. The swab was then immediately streaked over the surface of a rabbit blood agar plate. (The plate was divided into four portions: two for the cultures from the conjunctiva of each eye and the other two for the cultures from the lids.) For culture of material from the lids a swab was applied to the outer margin of the lid as the eye was held almost closed. Readings of the plates were made after eighteen and twenty-four and again after forty-eight hours' incubation at 37 C. The cultures from the conjunctivas and the lids were worked out separately. The colonies present were counted and the types of colonies studied.

If a staphylococcus was found, the following steps were carried out to determine its pathogenicity:

1. *Fermentation of Mannitol*—Colonies of staphylococci from the original blood agar plate were transferred to a 1 per cent Difco-phenolsulfonphthalein-mannitol agar plate. Fermentation may occur within a two to three hour period of incubation at 37 C. The presence of acid is indicated by the change of color from red to yellow.

2. *Coagulase Test.*—For this test fresh human plasma was used. The following procedure was carried out: Three-tenths cubic centimeter of plasma was mixed with a colony of staphylococci. The tube was incubated for four hours in a water bath at 37 C. Complete or partial coagulation after two to four hours indicates the production of coagulase.

Other types of organisms were isolated and identified by the usual bacteriologic tests.

MATERIAL AND RESULTS

This study included only eyes on which a cataract operation had been performed. Because only rarely was but one organism present and because we had many varieties from the conjunctiva and the lid, it was necessary to make an arbitrary decision with regard to the patient's bacteriologic classification. The cases were grouped roughly as follows:

Group 1 consisted of cases in which hemolytic and nonhemolytic Staphylococcus albus was the predominating organism. These strains did not ferment mannitol or produce coagulase.

Group 2 consisted of cases in which so-called pathogenic Staphylococcus aureus was found, though it did not necessarily predominate. The pathogenic Staph. aureus was defined by the fermentation of mannitol and the production of coagulase.

Group 3 consisted of cases in which so-called pathogenic Staph. aureus was found, though it did not necessarily predominate. The pathogenic Staph. aureus was defined by the fermentation of mannitol and the production of coagulase.

Groups 4, 5, 6, 7, 8, 9 and 10 consisted of cases in which the following organisms predominated: group 4, diphtheroids; group 5, Pneumococcus; group 6, Streptococcus pyogenes; group 7, Streptococcus viridans; group 8, Proteus vulgaris; group 9, Hemophilus influenzae, and group 10, miscellaneous gram-negative bacilli. Group 11 consisted of cases in which no growth occurred.

All variations of the bacteriologic pattern were found: In some cases one organism was present; in some three or more bacteria were present, and in others no growth occurred.

Our bacteriologic results and the correlation with the occurrence of purulent postoperative

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Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Jan. 15, 1945.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of Presbyterian Hospital.

1. Khorazo, D., and Thompson, R.: The Bacterial Flora of the Normal Conjunctiva, Am. J. Ophth. **18**: 1114-1116, 1935. Thompson, R., and Khorazo, D.: Susceptibility to Lysozyme of Staphylococci, Proc. Soc. Exper. Biol. & Med. **33**:299-302, 1935.

infection are shown in table 1. The table presents the data for eleven groups of cases according to the organisms isolated. Group 1 was the largest and the predominating organism isolated was hemolytic or nonhemolytic Staph. albus. The colonies presented morphologic variations. Some of the colonies were round and smooth; others had irregular edges and were opaque. A zone of hemolysis of from 1 to 2 mm. occurred in some instances. The pigment production varied from the typical white color to a slightly greenish shade. The organisms were most numerous in cultures from the lids, although in some cases the growths from the conjunctiva and from the lids were equal. This group of staphylococci was considered nonpathogenic, since the strains did not ferment mannitol or coagulate human plasma. In these cases no serious postoperative infections occurred.

TABLE 1.—*Correlation Between Preoperative Bacterial Flora and Postoperative Infection in 2,508 Cases in Which Neither Sulfonamide Drugs Nor Penicillin Was Used Preoperatively*

Group	Number of Operations	Organisms Isolated	Number of Postoperative Infections
1	1,706	Staph. albus	None
2	529	Pathogenic Staph. aureus	11
3	62	Unusual staphylococcus	None
4	86	Diphtheroids	None
5	23	Pneumococcus	None
6	9	Strep. pyogenes	None
7	6	Strep. viridans	None
8	16	Proteus vulgaris	None
9	2	H. influenzae	None
10	18	Gram-negative bacilli	None
11	52	No growth	None

Group 2 was comprised of cases in which preoperative cultures showed pathogenic hemolytic or nonhemolytic Staph. aureus. The colonial morphology was typical except for a few strains producing rough colonies. The hemolyzed zone was from 1.5 to 3 mm. in width. The usual pigment was orange; otherwise it varied from slightly yellow to deep yellow. Some species did not produce hemolysis. The staphylococci in this group were considered pathogenic, since the strains isolated fermented mannitol and produced coagulase. In this group postoperative infections with the Staph. aureus occurred in 11 cases. In 6 of these cases the eye was removed, while in the remaining 5 cases the globe was retained but all vision was lost. There were other complications in this group, such as persistent conjunctivitis, corneal ulcer and iridocyclitis, which may possibly have been produced by this organism, but they are not included in this report because of the difficulty in establishing the etiologic relationship.

Group 3 consisted of cases in which an atypical staphylococcus was the predominating organism. Strains isolated from the conjunctiva and the lids either fermented mannitol and did not produce coagulase or produced coagulase and did not ferment mannitol. The colonies isolated did not appear unusual when compared with those in the two groups previously described. No postoperative infection occurred.

Group 4 consisted of cases in which diphtheroids predominated. Some were identified as Corynebacterium xerose and others as Corynebacterium hofmanni. We did not attempt to classify all the diphtheroids. These organisms appeared to be entirely nonpathogenic for the eyes and did not produce any postoperative infections. Groups 5, 6 and 7, consisting of very few cases, were those in which Pneumococcus, Str. pyogenes and Str. viridans, respectively, predominated. No infections occurred postoperatively.

In groups 8 and 9 typical P. vulgaris and H. influenzae were the predominating respective organisms, and postoperative infections did not occur.

In group 10 gram-negative bacilli were present which were not classified. The colonies were translucent, round and glistening and developed fully only after forty-eight hours' incubation. They were gram-negative, slender bacilli, nonmotile, non-acid-fast and in some respects resembled diphtheroids morphologically. The strains isolated did not ferment any sugars and did not liquefy gelatin or Löffler's serum. Indole was not produced. Some strains produced acid, slight coagulation or digestion in litmus milk. Group 11 consisted of cases in which no growth occurred. In this group no postoperative complications occurred.

As seen in table 1, operation for cataract was performed in 529 cases in which pathogenic staphylococci were present. Since purulent postoperative infections occurred in only 11 cases, we thought that some specific surgical method might influence the incidence of postoperative infection. Several methods of cataract extraction were employed. The type most frequently employed was the intracapsular and next was the extracapsular extraction. Infection occurred in 5 cases after each of these types of extraction and in 1 case after a linear extraction. Therefore it seems that postoperative infection is independent of the type of operation.

Since these postoperative infections were due to pathogenic staphylococci, it seemed reasonable to investigate the possibility of developing a uniform preoperative procedure which could form the basis for treatment in the future. From

September 1943 to January 1944 two types of treatment to prevent postoperative infections were used. First, we applied an ointment (50 per cent hydrous wool fat and 50 per cent white petrolatum) containing sodium sulfathiazole in 5 per cent concentration three or four times daily to the conjunctiva and the lids until the pathogenic organisms disappeared. Repeated cultures determined the rate of progress of the treatment. It usually required from seven to ten days to eliminate the staphylococci, the period depending on the number of pathogens present on the lids and the conjunctiva. This treatment was discarded because of the frequency with which the patients exhibited an allergic response to this form of medication.

We then began using an ointment containing approximately 1,000 to 2,000 Oxford units of penicillin per gram of base (hydrous wool fat). After the isolation of a potential pathogen from the preoperative culture, this ointment was applied every two or three hours to the conjunctiva and the margins of the lids. The frequency of local application was based on the number of the bacteria present on the conjunctiva and the lids. Since penicillin deteriorates rapidly and also escapes from the eye, frequent treatments were considered necessary. In our opinion, it is not so satisfactory to use penicillin in drop form because in aqueous solution it disappears more rapidly from the conjunctiva and, furthermore, does not remain in constant contact with the eyelashes, where the greater number of organisms are usually found. To observe the rate of the clearing up of the infection, two cultures a day were taken: one in the morning and the other late in the afternoon. It was found that it required from three to eight days of constant treatment to eliminate the pathogenic staphylococci from the conjunctiva and the lids. This slow progress was confirmed by repeated cultures. In general the idea is to maintain the penicillin ointment constantly on the conjunctiva and the lids in order to inhibit the growth of the infecting organism. Each case presents an individual problem, depending on the number of organisms. In some cases a sensitivity to penicillin may develop, comparable to the sensitivity to the sulfonamide compounds. In such cases local treatment with penicillin ointment was discontinued. One patient appeared to be sensitive to the hydrous wool fat base.

All the strains of staphylococci isolated from the conjunctiva and the lids were tested for sensitivity to penicillin. The usual method of testing increasing dilutions of penicillin for its ability to prevent growth of a 1 : 100 dilution of staphylococci proved the organisms to be sensitive to the drug.

In 663 cases of cataract encountered since January 1944, penicillin ointment has been applied routinely to both eyes as soon as the material for cultures was taken. Each patient, before his operation, received at least five treatments, even in the absence of the pathogenic staphylococci. In the presence of a pathogenic staphylococcus, the penicillin treatment was continued as previously described until the conjunctivas and lids were free, or almost free, of pathogens. In not all the cases in which operation was done after the treatments were the eyes entirely free of the pathogens. The final cultures still had a few colonies either from the conjunctiva or from the lid. In these cases penicillin dressing was applied immediately after the operation and in the subsequent dressings. This group also includes the clinic cases, in which often cultures were taken about a week prior to admission. Because of the scarcity of penicillin ointment, the clinic patients were given ointment containing 5 per cent of sodium sulfathiazole, to be used several times daily. On admission to the hospital they were given the routine treatment with penicillin ointment. In none of the 663 cases did a purulent infection occur.

For comparison, we collected data on 730 earlier cases in which no preoperative cultures were made. The preoperative treatment here consisted of "puddling" the eye with a fresh solution of protein silver (25 per cent) an hour or two before operation and again on the operating table. In some instances this same treatment was used the night before operation and early the next morning, in addition to the two treatments just prior to operation. The incidence of purulent postoperative infection in the two groups is shown in table 2.

TABLE 2.—*Incidence of Postoperative Infections in 730 Cases in Which Preoperative Cultures Were Not Made and Only Protein Silver Was Used Before Operation as Compared with Incidence in a Series of 663 Cases in Which Preoperative Cultures Were Made and Penicillin Ointment Was Used*

Group	Number of Operations	Number of Infections	Preoperative Treatment
1	730	13	Protein silver, 25%
2	663	None	Penicillin ointment (1,000-2,000 Oxford units)

In 104 cases in which operation was delayed because of the presence of pathogenic organisms (as summarized in table 3) no infections occurred when this type of treatment was used

preoperatively to rid the conjunctiva and the lids of the bacteria. Some patients appeared to be sensitive to sulfathiazole; so they were treated with penicillin. Two patients from the penicillin group were placed under treatment with sulfadiazine because the pathogenic staphylococcus isolated from the conjunctiva was not sensitive to penicillin. Four patients, 2 with Str. pyogenes and 2 with a pneumococcus, were successfully treated preoperatively with an ointment containing 5 per cent sodium sulfathiazole. As seen in table 1, 32 patients with either Str. pyogenes or a pneumococcus present in the eye were not treated and no postoperative infection occurred.

COMMENT

From this bacteriologic analysis it would appear that the presence of a pathogenic staphylococcus in the eyes previous to cataract extraction increases the possibility of postoperative infection. Of 529 eyes operated on with known pathogenic staphylococci present in the preoperative cultures, purulent postoperative infections occurred in 11. It seems, also, that the type of operation does not influence the occurrence of postoperative infection. It is interesting to note that the great majority of the patients with cataract whose eyes showed numerous pathogens had no postoperative infection. It is possible that variation of lysozyme content has a great deal to do with the natural defense of the eyes and their resistance to postoperative infections. Fleming[2] and Ridley[3] stated that some pathogens are affected by lysozyme. It may be that a high concentration of certain enzymes affords protection against any type of infection. It is known that lysozyme may inhibit and destroy saprophytes. Tears have a high concentration of lysozyme. When postoperative infections developed, they were usually due to the pathogenic Staph. aureus. However, it is interesting to note that in the group of patients for whom preoperative cultures were not made the postoperative infections were not all due to Staph. aureus. In 2 the infection was caused by a pneumococcus, in 1 by Str. pyogenes and in 1 by Bacillus pyocyaneus.

Before preoperative treatment with penicillin or sulfathiazole was instituted, it was routine to "puddle" both eyes with 25 per cent protein silver. Thompson, Isaacs and Khorazo,[4] in a study of the action of this disinfectant under conditions as similar as possible to those in the eye, found that protein silver is slow in action as an antiseptic against pathogenic organisms and that it is moderately injurious to leukocytic activity and definitely so to the action of lysozyme.

Recently all patients with pathogenic organisms have been treated preoperatively with penicillin ointment or with 5 per cent sodium sulfathiazole ointment (table 3). Our experiments have shown that it is possible to free the conjunctiva of the pathogens in from three to ten days, and in some instances forty-eight hours is sufficient. While some patients normally carry pathogenic staphylococci in the conjunctiva or lids without any symptoms of inflammation and no infection develops if there is no surgical intervention, the presence of such pathogens in the eye may give rise to postoperative infection. Even this small series of patients treated locally with penicillin ointment shows such encouraging results that it should be possible to establish treatment in the future for patients whose conjunctiva and lids harbor pathogenic staphylococci. If this freedom from postoperative infection continues as the series is enlarged, the value of preoperative treatment is clearly suggested. It is interesting to note that in 27 of these 104 cases, foci other than the eye were found from which pathogenic staphylococci were isolated. These foci were in the throat, the nose and the skin around the eye. Adequate treatment of such foci may be necessary in order to prevent reinfection of the eye.

TABLE 3.—*Incidence of Postoperative Infections in 104 Patients Treated with Sulfonamide Drugs or Penicillin*

Number of Patients	Organisms Isolated	Drugs Used	Number of Postoperative Infections
72	Pathogenic Staph. aureus	Penicillin ointment (1,000-2,000 Oxford units per gram)	None
28	Pathogenic Staph. aureus	Sodium sulfathiazole ointment, 5%	None
2	Pneumococcus	Sodium sulfathiazole ointment, 5%	None
2	Str. pyogenes	Sodium sulfathiazole ointment, 5%	None

SUMMARY AND CONCLUSION

Great variation in the preoperative bacterial flora was observed in studies on 2,508 eyes

2. Fleming, A.: On a Remarkable Bacteriolytic Element Found in Tissues and Secretions, Proc. Roy. Soc., London, s.B **93**:306-317, 1922.

3. Ridley, F.: Lysozyme: An Antibacterial Body Present in Great Concentration in Tears, and Its Relation to Infection of the Human Eye, Proc. Roy. Soc. Med. **21**:1495-1506, 1928.

4. Thompson, R.; Isaacs, M. L., and Khorazo, D.: A Laboratory Study of Some Antiseptics with Reference to Ocular Application, Am. J. Ophth. **20**:1087-1099, 1937.

previous to operation for cataract. The predominating organism appeared to be Staph. albus, and the next in order pathogenic Staph. aureus. Other organisms occurred less frequently.

Postoperative infections were due in the great majority of cases to pathogenic Staph. aureus.

Postoperative infections observed were independent of the type of operation.

Of 730 cases in which no preoperative cultures were made and the treatment before operation consisted of instillation of protein silver, 25 per cent, three or four times in the twenty-four hours preceding operation, postoperative infection occurred in 13.

In 663 cases in which penicillin ointment (1,000 to 2,000 Oxford units), or sodium sulfathiazole ointment, 5 per cent, was used preoperatively, no infections occurred.

In 104 cases in which, because of known pathogenic organisms, operation was delayed until treatment with penicillin or sulfathiazole was used, no infections occurred.

This study indicates that preoperative cultures should be made on admission in every case in which cataract extraction is to be done, with a view to prophylactic treatment.

635 West One Hundred and Sixty-Fifth Street.

DISCUSSION

DR. ARNOLD KNAPP, New York: This is a valuable paper and shows a great advance in demonstrating that with certain preliminary treatment of the eyes preparatory to cataract extraction the convalescence will proceed without infection. Formerly one used to examine a smear, and if only a few staphylococci were present, the operation was proceeded with, provided everything else was normal. First, I should like to ask whether the number of staphylococci is a factor in pathogenicity. Second, I should like to ask Dr. Dunnington in how broad a sense he uses the term "infection." Does it include any undue redness of the eye or mild iritis? These also are signs of infection.

DR. JOHN DUNNINGTON, New York: I am glad that Dr. Knapp has brought up the question of what constitutes an infection, although I hoped I had made it clear that we included as "infections" only those conditions that went on to endophthalmitis or panophthalmitis. Most of the infected eyes were removed. All of them suffered complete loss of vision. We did not include as "infections" conjunctivitis, iritis, iridocyclitis or corneal ulcer, as there was genuine doubt as to whether we could identify the infecting organisms in such processes. In all of the cases listed as instances of infection cultures, both preoperative and postoperative, showed the infecting organism. We excluded purposely those in which there could be any question as to the nature of the infecting organism.

DR. D. LOCATCHER-KHORAZO, New York: In answer to the question as to how many organisms can incite an infection, we have seen infection develop when only 3 colonies of pathogenic staphylococci were found preoperatively.

CAVERNOUS DEGENERATION, NECROSIS AND OTHER REGRESSIVE PROCESSES IN OPTIC NERVE WITH VASCULAR DISEASE OF EYE

PROFESSOR ARNOLD LOEWENSTEIN
GLASGOW, SCOTLAND

Schnabel discovered cavernous degeneration in the tissue of the optic nerve in glaucomatous eyes. He [1] and his pupil Elschnig [2] declared that the condition was peculiar to glaucoma. Other investigators, like Axenfeld and Stock,[3] found cavernous changes in the nerve in cases of high myopia. Koyanagi and Takahashi [4] and other authors observed the condition in eyes excised for intraorbital tumor. Lagrange and Beauvieux [5] demonstrated pronounced vascular changes in glaucomatous eyes which showed cavernous degeneration of the nerve. In several cases of primary glaucoma they discovered sclerosis and obliteration of the laminar and retrolaminar vascular twigs in the optic nerve. It is interesting that they correlated cavernous degeneration of the optic nerve with similar features described in brain tissue in association with vascular disease, called by Pierre Marie *état lacunaire* and by C. and O. Vogt *état criblé*. It is likewise interesting that Duke-Elder [6] stated that an ischemic factor attendant on sclerosis of the nutrient arteries may cause softening of the optic nerve tissue in glaucomatous eyes.

Several explanations of cavernous degeneration in the nerve have been advanced. The first is that the condition is the result of increased intraocular pressure. Another view has it that an abnormal lytic process is at work, the lysins being liberated in the intraocular fluid of glaucomatous eyes (Elschnig). My findings lead me to think that these two views are untenable, for cavernous change is not limited to the prelaminar and the immediately postlaminar part of the nerve. For the most part the changes to be described are situated at some distance from the lamina cribrosa as well. A third view is that cavernous degeneration is the result of ascending degeneration in the nerve, a sequel of destruction of fibers at the disk associated with glaucoma. But, again, this cavernous change should present a continuity of the degeneration, and its intensity should be greatest near the disk and of lesser degree deeper.

I should like to stress that cavernous degeneration in the nerve is but one of the pathologic changes I have found in my study. The others were necrotic and sclerotic alterations. Thus, I found once ganglioform degeneration (cytoid bodies) and twice calcified hyaline concretions (drusen) within the tissue of the optic nerve. Sometimes, indeed, two processes were demonstrable in one section. Once an area of fatty infiltration was noted. Profound vascular changes were present in all the eyes examined. Most of the eyes had been removed for thrombosis of the central vein complicated by glaucoma.

Glaucoma and vascular disease are closely associated in one's mind. Wagenmann,[7] in 1892, stated the opinion that glaucoma and thrombosis of the central vein have a common cause. Salzmann,[8] after examining 65 eyes removed for absolute glaucoma, found that only 8 had a normal central retinal vein. He assumed that thrombosis of the central retinal vein frequently follows primary glaucoma. He confirmed the opinion of Schweigger, Hirschberg, Coats, Leber, Verhoeff and others. Salzmann assumed that a chain of cause (increase of intraocular pressure) and effect (thrombotic vascular processes) aggravates the primary condition.

All the eyes examined were removed at operation; so postmortem changes can be discounted.

From the Tennent Institute of Ophthalmology, Glasgow University (Prof. W. J. B. Riddell).

1. Schnabel, J.: Arch. f. Augenh. **15**:311, 1885; Ztschr. f. Augenh. **24**:273, 1892.

2. Elschnig: Glaukom, in Wessely, K.: Pathologische Anatomie des Auges, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928. vol. 1.

3. Stock, W.: Klin. Monatsbl. f. Augenh. **46**:342, 1908.

4. Koyanagi, Y., and Takahashi, T.: Arch. f. Ophth. **115**:596, 1924-1925.

5. Lagrange and Beauvieux: Arch. d'opht. **42**:129, 1925.

6. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1940, vol. 3, p. 3354.

7. Wagenmann, A.: Arch. f. Ophth. **38**:213, 1892.

8. Salzmann, M.: Glaukom und Netzhautzirkulation: Abhandlungen aus der Augenheilkunde und ihren Grenzgebieten, Berlin, S. Karger, 1933.

Nor does the result of trauma to the nerve inflicted by forceps or scissors (Siegrist,[9] Elschnig and Goldberg,[10] Spühler [11]) confuse the picture, for the effect of such injury bears no resemblance to the histologic changes described.

REPORT OF CASES

CASE 1.—The patient had a history of simple glaucoma, with trephination on Dec. 16, 1939, and cataract. Absolute glaucoma developed in September 1940. The eye was excised.

Fig. 1.—*A*, necrotic focus in front of and cavernous degeneration behind the lamina cribrosa. Here, *a* indicates a necrotic focus; *b*, a patch of necrotic nerve fibers; *c*, an engorged capillary; *d*, cavernous degeneration, and *e*, border tissue.

B, longitudinal section of a branch of the central artery. The arrow shows narrowing of the lumen at the sharp edge.

Examination revealed a broad synechia at the root of the iris on one side; cellular infiltration of the iris and ciliary body; occlusion of the pupil with pigmented organized tissue; engorgement of all uveal vessels, and extensive mossy hemorrhages in the periphery of the retina (the retina was examined in bulk). In anteroposterior sections the retinal cup was filled with glial tissue. There were small foci of cavernous degeneration in front of the cribriform plate and a necrotic process (fig. 1 *A*). The necrotic area (*a*) was sharply delineated, measured 80 by 100 microns and lay on the lamina.

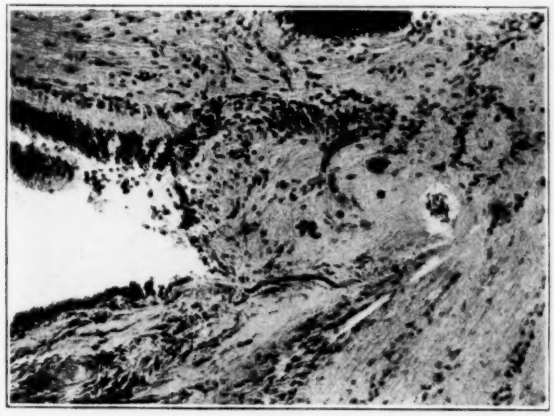

Fig. 2.—Necrotic prolapse of optic tissue between the retina and Bruch's membrane; *n* indicates a necrotic patch.

Fig. 3.—Four necrotic patches *1*, *2*, *3* and *4* in the lateral part of the optic nerve.

It reached the edge of the disk and was lined with what Elschnig has called "border tissue." A bundle of ill defined nerve fibers (*b*) was separated from the necrotic focus by infiltrated nerve fiber tissue. The walls of some of the small vessels in the nerve, as well as in the choroid, showed hyaline thickening. Behind the lamina there was extensive patchy cavernous degeneration (*d*). Figure 1 *B*, from the same eye, shows narrowing of the lumen of a branch of the central

9. Siegrist, A.: Arch. f. Augenh. (supp.) **44**:178, 1901.

10. Elschnig, A., and Goldberg, H.: Klin. Monatsbl. f. Augenh. **40** (pt. 2):81, 1902.

11. Spühler, O.: Arch. f. Ophth. **56**:77, 1903.

artery, from a diameter of 45 microns to one of 9 microns. The vessel is again dilated to a lumen diameter of 65 microns as it crosses the sharp edge of the cup.

CASE 2.—In the affected eye, thrombosis of the central retinal artery had occurred. The iris was atrophic and the retina hemorrhagic throughout, with cystic degeneration. The choroidal vessels were much engorged. All the vessels showed broad hyaline thickening of the walls. The retinal cup was filled with glial

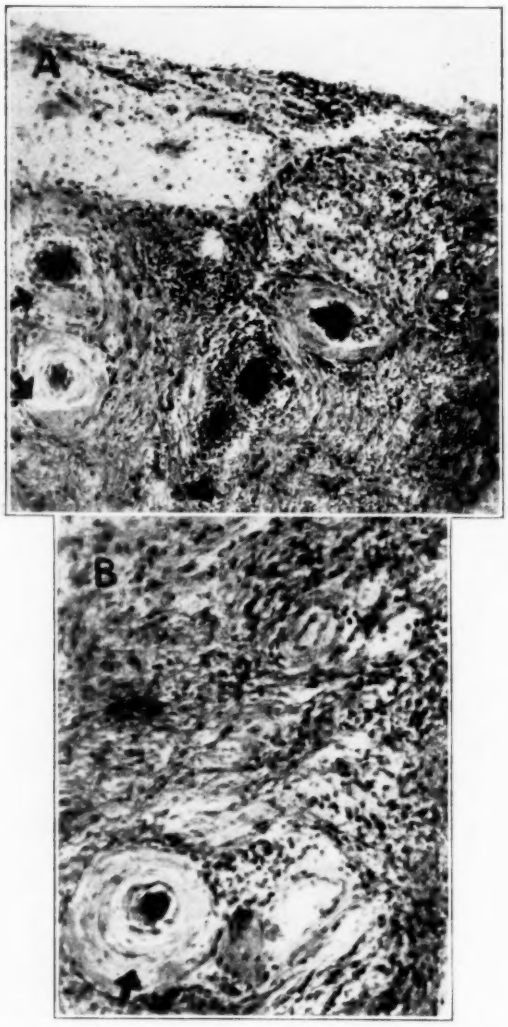

Fig. 4.—*A*, atheromatous vascular changes and cavernous degeneration. The arrows indicate atheroma vasculare.

B, high degree of thickening of the wall of the central retinal artery (arrow), surrounded by an area of cavernous degeneration. Note the ratio of lumen to wall of 1:2.

tissue and was bridged by a thin glial membrane. In figure 2, fibrous tissue with necrotic patches (*n*) can be seen to have invaded the area between Bruch's membrane and the retina, the layers of the latter having been raised in the process and destroyed at this side. This wedge of tissue was 225 microns in length and 170 microns in height. The center of this mass was largely necrotic. A vessel could be seen coursing around the end of Bruch's membrane, and this vessel showed endothelial proliferation. Around the necrotic area were several rows of glial cells and engorged capillaries. Elsewhere in the nerve, behind the lamina (fig. 3), were four necrotic patches. Partially or completely closed vessels were frequent in the neighborhood of these foci. The necrotic patches differed from the Siegrist-Elschnig artefacts.

CASE 3.—This case, again, is an instance of thrombosis of the central retinal artery with secondary glaucoma. Iridectomy was performed, without success. The eye was excised. The whole uvea was infiltrated, and the choroid was thickened to five or six times normal. The walls of the vessels of the choroid were broad and hyalinized, and many vessels in the retina, as well as in the choroid, showed fatty necrosis of the subendothelial layer. Sections stained with sudan III showed fatty masses in the outer molecular layer and in the optic nerve. In pyroxylin sections the optic nerve was richly infiltrated with lymphocytes and showed a minute, but widespread, "cavernous" change, giving the tissue a sievelike appearance (fig. 4 *A* and *B*). This change was not typical of cavernous degeneration but suggests fatty droplets dissolved in processing.

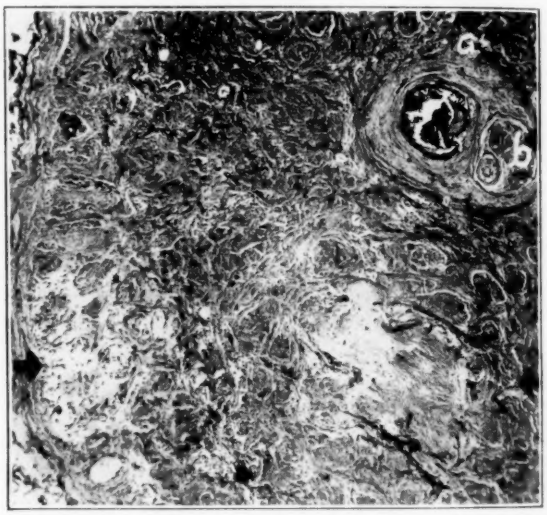

Fig. 5.—Cross section of the optic nerve behind the lamina cribrosa, showing the thrombosis of the central vessels. Weigert's elastica stain. Here, *a* indicates thickened perivascular coat; *b*, a thrombosed vein; arrow at right, a sclerosed plaque, and arrow at left, cavernous degeneration.

CASE 4.—The eye was seen in a stage of absolute glaucoma demanding excision. The patient suffered from associated cerebral vascular disease. Figure 5 shows extensive retrolaminar cavernous change. The process involves more than one third of the radius of the disk. There were two large cavernous areas of this type, which were not linked, as serial cross sections of the nerve proved. Figure 5 shows also a sclerosed plaque separated from the cavernous area by healthy tissue. The plaque is surrounded by thick elastic fibers. There was thickening of the pia and arachnoid, with subdural hemorrhages in the sheath of the optic nerve.

Case 5.—This case was one of advanced hypertensive retinopathy with widespread hemorrhages in all layers of the retina, fatty infiltration of the retina, ganglioform degeneration of the retinal nerve fiber layer and bilateral retinal detachment. The vessels showed marked endothelial proliferation and subendothelial fatty necrosis. The disk was swollen asymmetrically. The nerve fiber layer was thickened locally near the disk, a growth of glial cells being responsible (fig. 6 *A*). At the base of the swollen disk was a calcified, hyaline concretion, a so-called druse, measuring about 140 by 240 microns, staining dark blue and pushing the nerve fibers aside (fig. 6 *B*). Many of the nerve fibers ended blindly here. Small foci of cavernous degeneration appeared between the druse and the lamina. An area between the raised retina and the choroid was filled with a wedgelike mass of degenerated nerve fiber tissue. The cross section of this wedge was a triangle, with a length of 920 microns and a height of 270 microns. The mass consisted of poorly staining granular material with cytoid bodies. These bodies varied in size and the "pseudo nuclei" in staining reaction (fig. 6 *C*). The cytoid bodies did not take stains for fat. In this case different types of tissue degeneration were found existing simultaneously: necrotic, cavernous, ganglioform and hyaline.

Case 6.—This case was one of absolute glaucoma with iridocyclitis. The cornea, iris and ciliary body were infiltrated with lymphocytes and plasma cells. The root of the iris was adherent to the corneoscleral tissue. Strands of the vitreous with polymorphonuclear leukocytes and lymphocytes were observed. There was a preretinal capillary plexus, and extensive hemorrhage occurred throughout all layers of the retina. The septums and the sheaths of the optic nerve were infiltrated with lymphocytes. Necrotic foci occurred in front of the lamina, some 7 to 800 microns long by 3 to 400 microns broad (fig. 7 *A* and *B*), sharply demarcated and showing yellowish white in slides stained with hematoxylin and eosin. Around these foci was a framework of glial cells and fibroblasts. Most of the foci were structureless, granular masses. One focus sent a hornlike process between the retina and the pigmented epithelium, and at its outer limit it

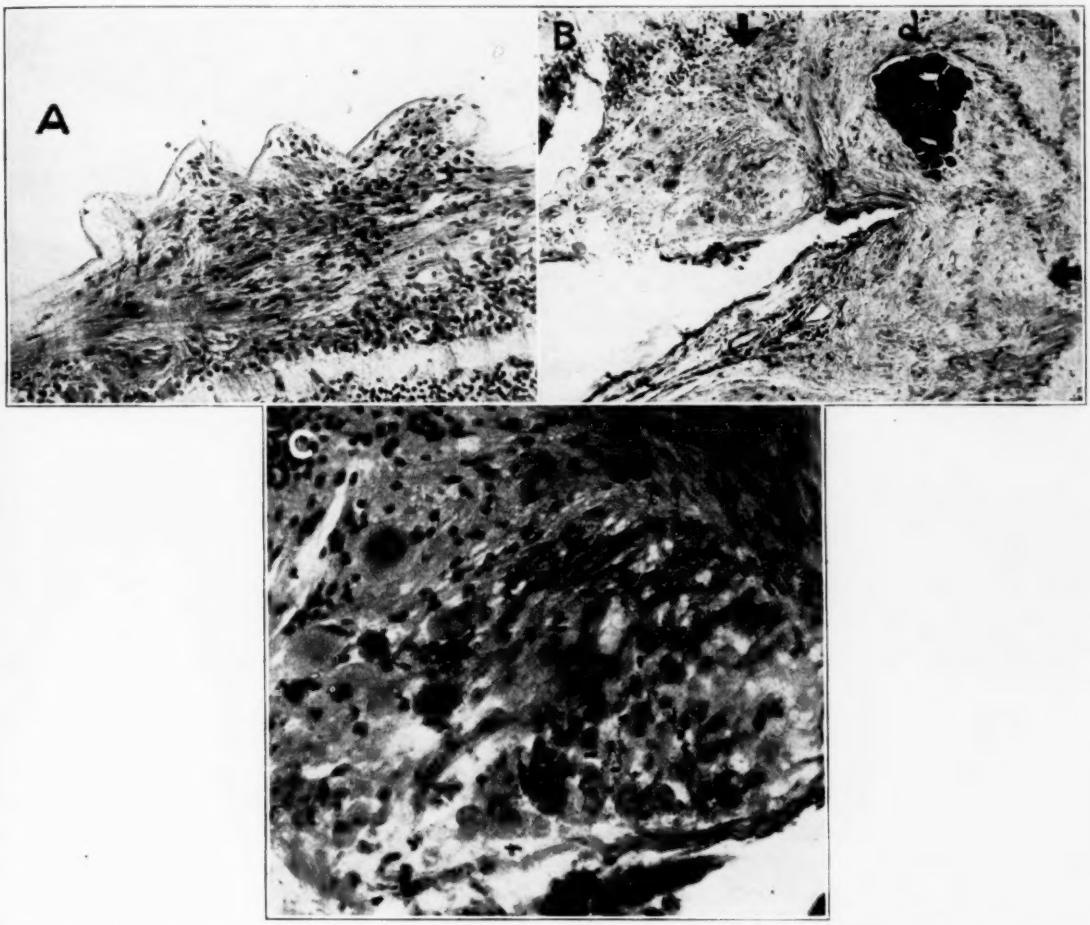

Fig. 6.—*A*, wavy protuberances near optic disk. The nerve fiber layer is thickened, and the glial nuclei are increased. *B*, subretinal prolapse of the nerve fibers which have undergone ganglioform degeneration (arrow at top) with calcified druse (*d*), or hyaline concretion, and cavernous degeneration (arrow at right). The retina is indicated by *r*. *C*, subretinal ganglioform degeneration of nerve fibers. Note the isolated nerve fibers diving into the necrotic mass. High power magnification.

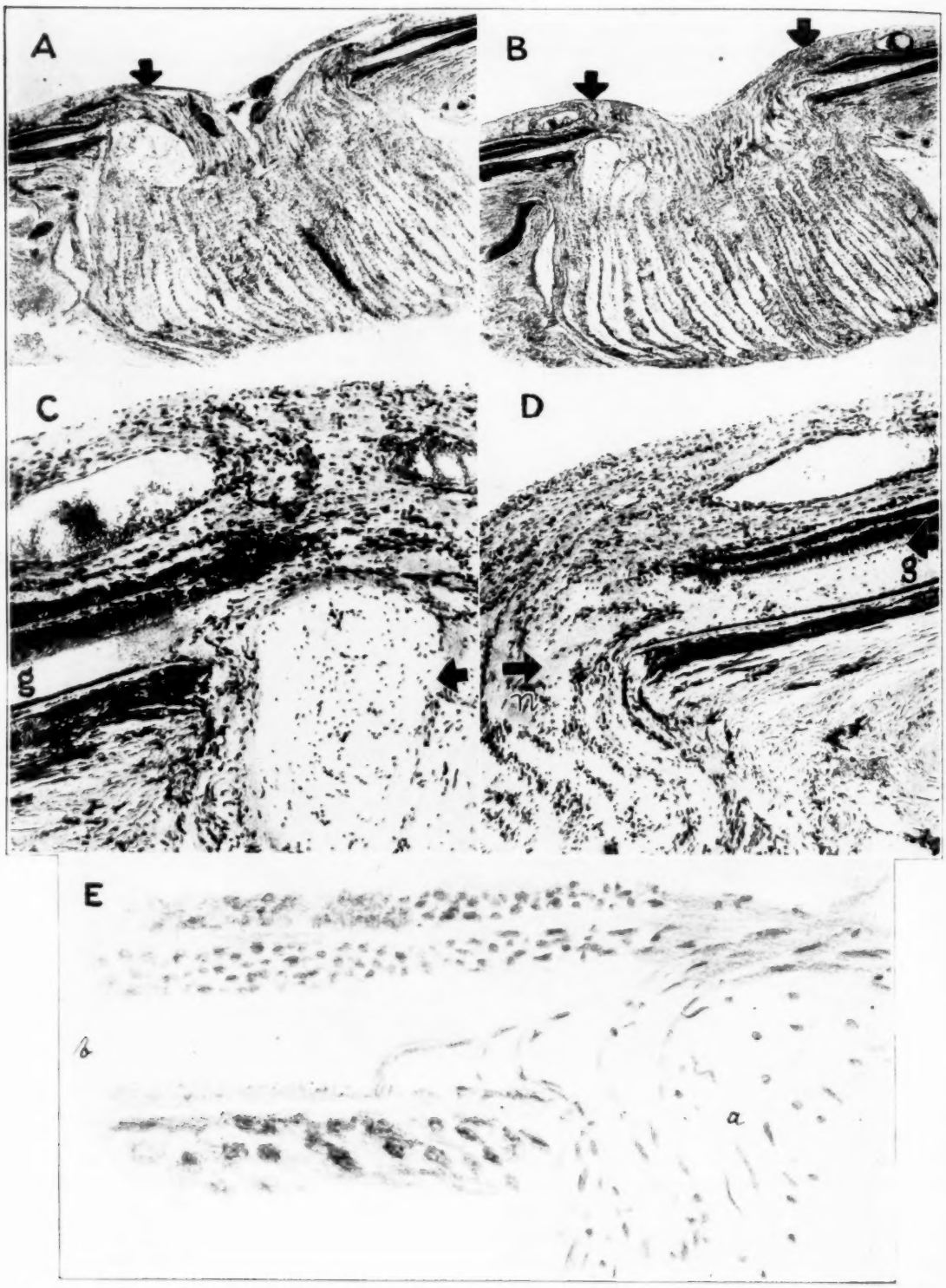

Fig. 7.—*A*, necrotic foci in the disk in front of the cribriform plate. The arrow indicates a sharply delineated necrotic focus with subretinal prolapse. *B*, necrotic foci (arrow at left) passing over into a subretinal necrotic mass (arrow at right). *C*, high power magnification of the necrotic focus (arrow at right) passing over into subretinal granular mass (arrow at left). *D*, nuclei of nerve fibers (*n*) turning sharply under the retina and ending abruptly within the necrotic layer. The arrow indicates normal neuroepithelium; *g*, the subretinal granular mass. *E*, necrotic mass (*a*) sending four processes into the subretinal granular mass (*b*); × 600.

was bound by a structure having a laminated arrangement, like the layers of an onion (fig. 7 *C* and *E*). The foci at the other side of the disk were not so sharply differentiated. There was an extension of granular necrotic substance subretinally. Here roots of elongated nuclei were freely embedded (fig. 7 *D*). The existence of an extensive retinal rete mirabile and the large retinal hemorrhage are, I think, evidence that venous obstruction was present in this case.

Several other eyes excised for glaucoma were examined histologically, but the details of the findings need not be given. Some of them showed degenerative changes in the nerve, mostly cavernous and necrotic, associated with profound vascular changes.

COMMENT

Two points engaged my attention as the result of the study of these 6 cases. The first, and less significant perhaps, is the occurrence of subretinal prolapse of optic nerve tissue as a result of disease processes in the nerve. This may be consequent on the growth of aberrant nerve fibers, such as I have described elsewhere (Loewenstein [12]). In that study, the aberrant nerve fibers were found growing out from the nerve into the retroretinal area in an eye excised for a melanotic growth. It is interesting to speculate that the pathologic outgrowth of nerve fibers and the melanoma may have sprung from one stem, namely, an abnormal neuroectoderm, if Masson's concept is correct. Another concept more to the point is the origin of this prolapse of optic nerve tissue, such as occurred in case 5 (hypertensive neuroretinitis). It is suggested by a consideration of the changes that take place in papilledema. Paton and Holmes [13] have shown that the optic nerve fibers sometimes push aside and raise the retina in the neighborhood of the swollen disk. B. Samuels [13a] has distinguished three types of circumpapillary tissue in papilledema: (1) a more or less homogeneous mass, similar to a coagulated fluid; (2) a very loosely meshed tissue, poor in nuclei, and (3) a compact, very cellular tissue, reminding one of neuroglia proliferation. Abelsdorff,[14] in similar observations, described the fibers at the edge of the swollen disk as assuming an S-shaped band. Paton and Holmes were able to demonstrate an actual rupture of the fibers in this lateral bulge. I did not note rupture of the fibers in 6 cases of papilledema, other than in case 5, in which I examined the eyes. In 1 case only a broad wedge of optic nerve fibers was found between the hexagonal cells and the retina. It would seem, however, that in case 5 (hypertensive retinopathy) rupture of the fibers really took place in passing over the sharp edge of the calcified mass. The rupture may have been due to the mechanical effect of the lesion.

The second, and major, point of interest is the variety of forms of degeneration appearing consistently in the nerve in association with profound vascular disease. Various degenerative processes were often present contemporaneously. Necrotic and cavernous patches were frequently associated. Case 4 is especially interesting, as several cavernous foci occurred, with a sclerosed plaque. Small vessels of the optic nerve showed changes in the walls and thrombotic occlusion. This association was stressed recently by Scheinker,[15] who demonstrated that the sclerosed plaques in the brain in cases of acute disseminated sclerosis are frequently associated with thrombosed vessels.

I want to mention especially the findings in case 3, in which fatty infiltration of the optic nerve tissue was discovered with the sudan III stain. Pyroxylin sections of the other part of the optic nerve displayed rarefaction of the tissue, similar to cavernous changes.

Henschen [16] found malacic and necrotic changes associated with arteriosclerosis. He demonstrated them in the occipital lobe and elsewhere. Fuchs [17] discovered focal degeneration in the optic nerve in cases of arteriosclerosis. The foci appeared as granular masses in section without inflammatory reaction. Fuchs stated that they were consequent on disturbance of the small pial twigs supplying the nerve. In the histologic literature on toxic neuritides, e. g., those due to alcohol and diabetes, vascular changes are frequently mentioned (Igersheimer [18]). I think that the changes I have found in the optic nerve—cavernous, necrotic, ganglioform and sclerosed degeneration and establishment of calcified drusen—were secondary to vascular disease.

SUMMARY

A histologic study was made of several eyes with profound vascular changes. Special attention was given to the pathologic types of degen-

12. Loewenstein, A.: Brit. J. Ophth. **29**:6, 1945.

13. Paton, L., and Holmes, G.: Tr. Ophth. Soc. U. Kingdom **31**:117, 1911; Brain **33**:389, 1911.

13a. Samuels, B.: The Histopathology of Papilloedema, Tr. Ophth. Soc. U. Kingdom **57**:529, 1938.

14. Abelsdorff: Optic Nerve, in Wessely, K.: Pathologische Anatomie des Auges, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 1, p. 725.

15. Scheinker, I. M.: Histogenesis of Early Lesions of Multiple Sclerosis: Significance of Vascular Changes, Arch. Neurol. & Psychiat. **49**:178 (Feb.) 1943.

16. Henschen, S. E.: Arch. f. Ophth. **78**:212, 1911.

17. Fuchs, E.: Arch. f. Ophth. **103**:304, 1920.

18. Igersheimer, J.: Am. J. Ophth. **23**:1243, 1940.

eration in the optic nerves. The observations on 6 eyes are described in some detail.

Cavernous and necrotic degeneration were almost consistently found, and frequently the two changes occurred together. They were sometimes present in marked degree; at others they were inconspicuous. A sclerotic plaque, a subretinal process of ganglioform degeneration of nerve fibers and, in 2 cases, a calcified druse were found in the optic nerve.

In some cases the disease process exceeded the boundaries of the nerve head and extended into the subretinal space.

These observations lead me to conclude that all these degenerative changes are the result of vascular damage with impairment of nutrition rather than the effect of increased intraocular pressure.

Tennent Institute of Ophthalmology.

EFFECT OF ANOXIA ON HETEROPHORIA AND ITS ANALOGY WITH CONVERGENT CONCOMITANT SQUINT

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In a previous paper [1] the existing knowledge of the voluntary and motor mechanisms controlling ocular movements was summarized. It was pointed out that the reflex mechanism was even more important than the voluntary, in that the eyes were constantly under the influence of involuntary tonic impulses which determined not only their fixation of objects in space but also their relation to each other. This mechanism is the harness which keeps the eyes associated so that the two maculas are used simultaneously.

The chief source of reflex tone is the visual fixation reflex. Lancaster [2] pointed out some time ago the importance of this mechanism for fusion, although he considered that it was a conscious, voluntary mechanism and traced the afferent pathway from the frontal centers instead of from the optomotor center in the occipital cortex. The evidence I believe is strongly in favor of its being a purely involuntary reflex.

All of the other sources of tone, such as the otolith apparatus, the semicircular canals, the convergence mechanism, and perhaps others as yet undiscovered, together with the visual fixation reflex suffice to keep the eyes in alinement with each other and fixed on an object in space which falls within the visual and motor fields. When the visual fixation reflex is artificially eliminated by one means or another and the position of the eyes is measured one is determining the effect of all these other sources of tone working together. This is spoken of as the measurement of the muscle balance, which, as Lancaster aptly remarks, puts the emphasis on the wrong part of the neuromuscular apparatus. I cannot do better than quote from Lancaster's admirable paper as follows:

> He [the average ophthalmologist] sees an exophoria and says that the lateral rectus muscles are pulling too hard or that the mesial rectus muscles are not pulling hard enough, which is true. But he jumps to the naive conclusion that the former muscles are too strong or the latter too weak, whereas the muscles are probably faithfully carrying out the orders brought to them by the nerves. The nerves, for their part, are merely transmitting the impulses from the nuclei, and the nuclei are issuing only such orders to contract or to relax as the messages from the supranuclear centers call for.
>
> Any part of this neuromuscular mechanism may be out of order, and more than one part may be affected. But is it not reasonable to think that the most complicated part is the most likely to be acting imperfectly? When the patient is put through a course of orthoptic training, is it reasonable to suppose that the chief factor is a strengthening of the muscles already one hundred times as powerful as the task calls for? Does Paderewski play the piano so much better than another person because his muscles are stronger?

He also says:

> The sum of the matter is that nerve stimuli are constantly flowing to the extra-ocular muscles, and the stream varies with varying conditions. The resultant tonus or contraction of the twelve muscles does not produce a perfect balance, and the fusion faculty has to correct any shortcomings. When fusion is eliminated the ophthalmologist is able to see how much work the fusion faculty was doing before he covered one eye or otherwise eliminated fusion. This is the important thing about heterophoria—it shows what the task of the fusion faculty is. The measurement of the amplitude of fusion shows the capacity of the fusion faculty to deal with this.[3]

One must conclude therefore that heterophoria is an indication that the remaining reflex sources of ocular muscle tone have failed to keep the eyes in perfect alinement when the fusional mechanism is eliminated. "Orthophoria, the ideal condition, is probably never found in all the positions in which the eyes are habitually used, and should therefore not be thought of as the normal condition. The limits within which there may be deviations from this ideal without symptoms are well recognized clinically, however, and it is certainly too much to expect ocular comfort in a person whose fusional impulses have to keep under control a latent deviation of the visual axes of more than 1 prism diopter in the vertical, or of more than 4 in the horizontal, plane for distance.

From the Hospital of the University of Pennsylvania.

Address delivered before the New England Ophthalmological Society, Boston, Feb. 20, 1945.

1. Adler, F. H.: Pathologic Physiology of Convergent Strabismus: Motor Aspects of the Nonaccommodational Type, Arch. Ophth. **33**:362 (May) 1945.

2. Lancaster, W. B.: Physiology of Disturbances of Ocular Motility, Arch. Ophth. **17**:983 (June) 1937.

3. Lancaster,[2] p. 991.

Since fusion is imperfect at birth the position the eyes assume until this mechanism develops into full maturity is usually a heterophoric position. It can easily be determined that at this period all the sources of reflex tone are active and variable and seldom are sufficient to hold the eyes in alinement. Frequently the eyes will deviate from one another during the first year of life, one eye remaining fixed while the other moves out or in or in the vertical direction. These movements are slow, steady deviations, which betrays their reflex nature.

If fusion should never develop the position assumed by the eyes would be that dictated by the remaining sources of reflex tone. It would not be the so-called position of rest, which occurs only during deep sleep, anesthesia or death. This position, which is generally divergence and some sursumvergence, never occurs as a result of elimination of the visual fixation reflex alone. This fact and a great many others which need not be mentioned here should throw doubt on the importance of a deficiency or absence of fusion as the primary cause of comitant strabismus. It is true that strabismus may not occur because of good fusion, in which case the condition will remain a heterophoria throughout life. But the absence of fusion without a preexisting heterophoria will never produce squint. The primary cause of squint is heterophoria, and by definition comitant strabismus is a manifest heterophoria.

The search for the cause or causes of squint therefore resolves itself into a search for the cause of the heterophoria. In the case of the lateral squints this must be sought in disorders of the convergence and divergence mechanism. Unfortunately, little is known of these mechanisms, even of their anatomic pathways.

There is no known frontal center for either convergence or divergence, although convergence certainly can be initiated volitionally. Involuntary convergence and divergence can easily be demonstrated under the influence of the visual fixation reflex, by merely inserting small prisms base in or out in front of one eye while looking at a muscle light. Without any effort on the subject's part the eye will immediately make an inward or outward movement in the interest of fusion until the image lies on the macula once more. This movement is involuntary—it cannot be prevented even by a willed effort. The largest prism which still effects this movement reflexly is the measure of the reflex fusional convergence or divergence.

Practically nothing is known of the normal physiology of the convergence and divergence mechanism, and even pathologic conditions have served to throw little light on its function. Convergence spasm usually occurs in neurasthenic persons,[4] but the mechanism which seems to be at fault here is the voluntary convergence rather than the reflex mechanism. Divergence paralysis is a recognized clinical entity, but since most of these patients eventually show paralysis of both external rectus muscles one cannot be sure that a separate divergence mechanism is concerned.

The association of convergence and accommodation during the act of looking at close objects develops a normal linkage between these two functions. An abnormal amount of hyperopia calls for excessive convergence and readily explains the development of the esophoria which leads to accommodative convergent squint. About one third of convergent squints are purely accommodative. Another third have an accommodative element, but are probably not due solely to an abnormal hyperopia. There remain nearly a third of the cases of convergent squint which are not paralytic and which, like the accommodative squints, are due to an abnormal tonic convergence. The reason for this abnormal tonus is unknown, however.

Flight Schedule

	Feet	Meters
7:34 p. m.	started ground level	
7:35 p. m.	2,000	600
7:36 p. m.	7,000	2,100
7:37 p. m.	12,000	3,600
7:45 p. m.	16,000	4,800
8:26 p. m.	18,000	5,400
8:52 p. m.	descent started	
9:44 p. m.	3,000	900
9:47 p. m.	0 ended	

It has been known for some time that under the influence of alcohol there develops an increasing esophoria, which eventually may be sufficient to overcome the fusional fixation reflex and produce esotropia. This occurs in all persons, regardless of whether they were orthophoric, esophoric or exophoric before partaking of the alcohol. Carefully controlled studies have been reported by Powell[5] and by Colson.[6] These authors are not decided as to the cause of the esophoria, whether it is due to an increase in

4. Souders, B. F.: Hysterical Convergence Spasm, Arch. Ophth. **27**:361 (Feb.) 1942.

5. Powell, W. H., Jr.: Ocular Manifestations of Alcohol and Consideration of Individual Variations in Seven Cases Studied, J. Aviation Med. **9**:97 (June) 1938.

6. Colson, Z. W.: Effect of Alcohol on Vision: Experimental Investigation, J. A. M. A. **115**:1525 (Nov. 2) 1940.

convergence tone or whether there is a weakness of the divergence mechanism.

A similar development of esophoria has been found to occur from the effect of anoxia by Velhagen.[7] Working in a low pressure chamber he found that the muscle balance changed in the direction of esophoria as the atmospheric pressure was reduced, no matter what the subject's phoria was to begin with. Since this was contrary to what Berens and Wilmer[8] had previously reported, I decided to repeat these experiments. The latter authors had found that anoxia merely increased any phoria which was present at ground level; i. e., if the subject had an exophoria to start with it became greater with anoxia, and similarly esophoria increased.

The experiments reported here were made in the low pressure chamber of the Medical School of the University of Pennsylvania through the courtesy of, and with the able assistance of, Dr. Martin Larrabee.

Eight normal subjects had their muscle balance for far and near measured by the Maddox rod and phoropter and for near again with the Maddox wing test. Their involuntary fixation reflex was then measured for both convergence and divergence, care being taken to measure the reflex vergences only and not the voluntary ductions. (The reflexes vergences are measured by inserting prisms of increasing strength in front of one or both eyes while both are fixing a distant light. When the subject first sees two lights without making any effort to fuse them the strength of prism used is the measure of the reflex vergence.) The fusional amplitude of each subject was then measured on the orthoptoscope. (The fusional measurements were all made by Miss Elizabeth Jackson, the Orthoptic Technician of the University of Pennsylvania Hospital.)

As soon as the initial measurements were made at ground level the pressure in the chamber was reduced to that corresponding to 16,000 feet (see flight schedule) and the measurements were repeated.

This was done again at 18,000 feet. The descent was then made to ground level, and the measurements were again repeated. During the flight only the observers wore oxygen masks. The experimental subjects showed all the signs of fairly severe anoxia toward the end of the run. One subject had to be given oxygen at 18,000 feet.

Table 1 gives the data of all the tests save those of fusional amplitude. In the first column

TABLE 1.—*Data for All Tests Except Those of Fusional Amplitude*

Name	Altitude, Feet	Distance Maddox Rod		Near Maddox Rod		Near Maddox Wing		Ductions	
		Eso-phoria	Exo-phoria	Eso-phoria	Exo-phoria	Eso-phoria	Exo-phoria	Abduction	Adduction
Crandall	0	3.5	..	3.5	..	0	0	9	30
8:12 p. m.	16,000	5.5	..	0	0	..	1	8	40
8:48 p. m.	18,000	8	..	1	..	0	0	5	40
9:51 p. m.	0	4	..	2.5	..	0	0	10	36
Mayock	0	..	1	..	1	..	3	6	18
7:57 p. m.	16,000	1	..	0	0	..	2	5	16
8:39 p. m.	18,000	3	..	..	1	..	1	6	18
9:50 p. m.	0	2.5	..	0	0	..	3	7	26
Shorey	0	..	1	..	8	..	5	8	4
8:05 p. m.	16,000	1	..	..	4	..	2	8	5
8:33 p. m.	18,000	1.5	..	..	3.5	..	3	6	4
9:44 p. m.	3,000	..	1.5	..	3.5	..	5	6	4
Leopold	0	2	..	..	1.5	0	0	6	54
8:07 p. m.	16,000	0.5	..	..	4	..	1	7	60+
8:30 p. m.	18,000	1	..	..	5	..	2	9	54
10:01 p. m.	0	2	..	0	0	1	..	14	42
La Motte	0	1	..	1	..	3	..	4	50
7:45 p. m.	16,000	3.5	..	6	..	..	2	4	64
8:45 p. m.	18,000	7	..	6	..	..	2	—2	30
10:03 p. m.	0	2.5	..	5	..	..	2	8	59
Steele	0	2	..	..	5	0	0	6	16
8:02 p. m.	16,000	1	..	..	4	..	1	6	18
8:33 p. m.	18,000	6	..	..	2	..	1	3	17
9:53 p. m.	0	3	..	..	1	..	1	5	15
Wheeler	0	0	0	..	1.5	..	2	10	10
8:00 p. m.	16,000	1	..	..	4	..	2	8	13
8:20 p. m., given oxygen									
9:47 p. m.	0	1	..	..	2	..	2	8	7
Corneal	0	7	..	..	1	1	..	2	16
7:51 p. m.	16,000	4.5	..	0	0	1	..	0	16
8:41 p. m.	18,000	9	..	..	4	Unreliable	..	—4	Unreliable
9:50 p. m.	0	2	..	0	0	1	..	4	25

7. Velhagen, K., Jr.: Heterophorie unter den Bedingungen des Höhenfluges, Luftfahrtmedizin **1**:344, 1937.

8. Wilmer, W. H., and Berens, C., Jr.: V. The Effect of Altitude on Ocular Functions, J. A. M. A. **71**:1397 (Oct. 26) 1918.

is the name of the subject and the time at which his readings were taken, at various altitudes, which are given in the next column. The figures in the following columns are prism diopters, and are self explanatory.

In every case but 1 (Leopold) there was a change in the phoria for distance in the direction of esophoria, regardless of whether the subject

TABLE 2.—*Fusion Tests on Orthoptoscope (Grade III Slides)*

Name	Altitude, Feet	Abduction		Adduction	
		Recovery	Point	Recovery	Point
Crandall	0	— 8	— 4	+50	+28
	16,000	— 8	— 2	+56	+28
	18,000	0	+10	+58	+34
	0	— 5	0	+50	+34
Mayock	0	— 5	— 3	+26	+11
	16,000	— 2	0	+28	+18
	18,000	+ 2	+ 8	+32	+20
	0	— 2	+ 2	+32	+18
Leopold	0	— 4	— 1	+50	+21
	16,000	— 8	0	+52	+24
	18,000	— 4	+ 4	+50	+22
	0	— 8	+ 4	+64	+32
Shorey	0	— 9	— 6	+16	+11
	16,000	— 4	+ 2	+30	+14
	18,000	— 1	+ 6	+ 6	+ 4
	0	— 7	— 3	+14	+10
Steele	0	— 5	— 3	+45	+15
	16,000	— 2	+ 4	+30	+20
	18,000	+ 4	+ 4	+40	+12
	0	— 4	0	+26	+15
Wheeler	0	— 3	0	+26	+13
	16,000	— 8	0	+30	+10
	18,000	....	....	....	....
	0	— 4	— 2	+30	+10
Corneal	0	+ 7	+15	+31	+17
	16,000	+ 6	+14	+28	+12
	18,000	....	....	....	....
	0	— 1	0	+30	+11
La Motte	0	— 1	+ 9	+60	+39
	16,000	— 2	+20	+66	+58
	18,000	— 2	+20	+60	+48
	0	— 2	+ 4	+80	+50

was esophoric or exophoric to start with. In this exception it will be noticed that the subject was exposed the shortest period of time to the 18,000 foot level. (Compare time table of flight with time of his examination at 18,000 feet. The 18,000 foot level was reached at 8:26 p. m. and Leopold was tested at 8:30 p. m. He had been exposed to this level for only four minutes.) Corneal and La Motte, who were esophoric to start with, became esotropic.

The changes in phoria at 33 cm. were not so striking or so constant. The same results were obtained with the Maddox wing test as with the Maddox rod for near. Some of the subjects became more esophoric (or less exophoric) and some did just the reverse. The involuntary vergences showed a lessening of divergence and some increase in convergence. These tests were difficult to carry out in the severely anoxic subjects, and although they point in the same direction as the fusional tests they are not so reliable.

Table 2 gives the results of the tests for fusion done on an orthoscope. From this table the range of fusion was obtained. The figures for this appear in table 3.

In the interpretation of these results certain factors should be taken into account. These are as follows:

1. Familiarity with the test tends to increase the fusion range. Therefore no significance should be attached to the difference between the figures before and after the flight.

2. Convergence tends to increase with repetition.

3. The effect of voluntary effort is less in abduction and at a minimum in abduction-recovery.

4. The fusion range between the breaking points is larger than between the recovery points because stimuli of identical images involuntarily keep the eyes associated as the images

TABLE 3.—*Range of Fusion on Orthoptoscope (Grade III Slides)*

Name	Altitude, Feet	Breaking Points	Recovery Points
Crandall	0	— 8 to +50	— 4 to +28
	16,000	— 8 to +56	— 2 to +28
	18,000	0 to +58	+10 to +34
	0	— 5 to +50	0 to +30
Mayock	0	— 5 to +26	— 3 to +11
	16,000	— 2 to +28	0 to +18
	18,000	+ 2 to +32	+ 8 to +20
	0	— 2 to +32	+ 2 to +18
Leopold	0	— 4 to +50	— 1 to +21
	16,000	— 8 to +52	0 to +18
	18,000	— 4 to +50	+ 4 to +22
	0	— 8 to +64	+ 4 to +32
Shorey	0	— 9 to +16	— 6 to +11
	16,000	— 4 to +30	+ 2 to +14
	18,000	— 1 to + 6	+ 6 to + 4
	0	— 7 to +14	+ 3 to +10
Steele	0	— 5 to +45	— 3 to +15
	16,000	— 2 to +30	+ 4 to +20
	18,000	+ 4 to +40	+ 4 to +12
	0	— 4 to +26	0 to +15
Wheeler	0	— 3 to +26	0 to +13
	16,000	— 8 to +30	0 to +10
	18,000	.....	.....
	0	— 4 to +30	— 2 to +10
Corneal	0	+ 7 to +31	+15 to +17
	16,000	+ 6 to +28	+14 to +12
	18,000	.....	.....
	0	— 1 to +30	0 to +11
La Motte	0	— 1 to +60	+ 9 to +39
	16,000	— 2 to +66	+20 to +58
	18,000	— 2 to +60	+20 to +48
	0	— 2 to +80	+ 4 to +50

are moved in or out. Once they are dissociated fusion does not commence until the eyes are inside the range where fusion is easiest.

5. The range of the recovery points is therefore the most accurate index of true fusional ability.

The tests show that the abduction recovery points in 6 out of 8 persons show a consistent shift toward convergence with anoxia. (The 2 who did not conform were unreliable at 18,000

feet in this and in the other tests.) The 6 men showed a return toward the divergent position on restoration of oxygen. Only 1 returned as far as his original measurements.

Convergence increases fairly proportionately to the lessening of the divergence, so that there is little change in the range of fusion.

The fusional convergence tends to remain constant or even increase on return to oxygen. This is attributable to repetition and familiarity with the test. If the range of fusion is abnormally low, as it was in 2 cases, it tends to break entirely with anoxia. (Shorey was exophoric —6 to +11, and at 16,000 feet showed the normal change to +2 to +14. At 18,000 feet an abduction recovery point was obtained at +6, but recovery of range of fusion was entirely lacking. Corneal was esophoric + 15 to + 17 and broke from esophoria to esotropia at 16,000 feet and his recovery fusion range at 16,000 feet was absent. No reliable data could be obtained at 18,000 feet.)

From these data one can conclude that during lack of oxygen there is a shift of the range of fusion toward the convergent position. The range itself shows little change in the normal subject if the range is normal at ground level. If the range is abnormally small to begin with, it may be wiped out altogether, and homonymous diplopia may develop.

The development of esophoria under the influence of alcohol and anoxia is due either to an increase in convergence tone or to a diminution of divergence tone. There is no evidence in the literature or in the data presented here which points strongly to either assumption. Velhagen was forced to conclude that some change must occur in the muscles themselves, but this seems unlikely due to the fact that there is no incomitance or anisophoria. All the evidence points to a change in a supranuclear mechanism.

Alcohol is thought to act by depressing the higher centers, and any apparent stimulation results from the "unrestrained activity of lower centers freed by the depression of higher inhibitory control mechanisms.[9]" One may assume, therefore, that the convergence mechanism is normally inhibited by higher centers, which alcohol and anoxia remove. There is a parallel example of this in the case of the pupil. During the third stage of anesthesia due to ether and chloroform, the pupil constricts, and this constriction is supposed to be due to the abolition of cerebral impulses which normally inhibit the tone of the oculomotor constrictor center, i. e., the Edinger-Westphal nucleus.[10] It has also been claimed that during plane 3 of the third stage of anesthesia the eyes are fixed in the convergent position. These forced movements and changes in posture of the eyeballs under general anesthesia have never been satisfactorily studied, and should give some clue to the behavior of the mechanism under discussion.

The esophoria produced by alcohol and anoxia, which may even become esotropia, may not be the same as that which occurs in early childhood and which leads to comitant squint, but there is enough similarity in the two conditions to study squint from this point of view. Both are caused by some interference with a supranuclear mechanism. The comitance of squint proves that the condition is of supranuclear origin. One must keep in mind the fact that comitance may be lost, however, because of lack of use of a squinting eye, and some squints will be labeled incomitant at first because the squinting (and usually amblyopic) eye fails to turn to the temporal side completely. In these cases patching the good eye will usually break up not only the amblyopia but also the incomitance, and the angle of squint will become the same in all directions of gaze. The diagnosis of incomitance should not be made therefore until every effort has been made to break up this motor inhibition.

Chavasse speaks of true paralytic squint losing its incomitance after there is partial recovery, and becoming comitant, but I do not believe that this ever happens, unless, of course, there is complete recovery from the paralysis, and then the squint will disappear. As long as there is weakness of a muscle there will be incomitance. The recovery of function may be sufficient to enable the muscle to pull the eye out completely, but the sound eye will invariably show overshooting (secondary deviation) in this field of action, and thus betray the paralytic origin of the squint.

SUMMARY

The eyes are harnessed together by many reflex sources of tone. The chief source of reflex tone is the visual fixation reflex, which serves to keep the two foveas lined up with the object of regard. The cortical center for this reflex lies in area 17, and possibly areas 18 and 19, of Brodmann, and may be thought of as the motor part at least of a true fusion center. Heterophoria is the position the eyes assume when the visual fixation reflex is broken up. The position the

9. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, p. 109.

10. Goodman and Gilman,[9] p. 41.

eyes then assume is due to the sum of all the other sources of reflex tone. These are all from supranuclear mechanisms.

The primary cause of comitant squint is heterophoria, and comitant squint is a manifest heterophoria. The cause of comitant squint must be sought in the cause of the heterophoria. The cause of accommodational squints is known. Many other convergent comitant squints are not accommodational, and as yet nothing is known of their cause.

Alcohol and anoxia produce an esophoria for distance and a shift in the range of fusion toward convergence, and if severe enough may result in a convergent comitant squint. The nonaccommodational convergent comitant squints of childhood should be considered as similar conditions caused by an excessive convergence tone and should be investigated from this point of view. No claim is made that the two conditions are in any way identical.

Clinical Notes

INTERSTITIAL KERATITIS TREATED WITH SUBCONJUNCTIVAL INJECTIONS OF PENICILLIN

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The following case of interstitial keratitis is of interest because the progress of the disease was apparently checked by the use of subconjunctival injections of penicillin. No report has been found in the literature of the treatment of interstitial keratitis with subconjunctival injections of penicillin. General antisyphilitic therapy did not seem indicated because the patient had received adequate general treatment for syphilis prior to the beginning of the keratitis. The corneal infiltration and vascularization progressed rapidly until subconjunctival injections of penicillin were used.

REPORT OF A CASE

Mr. A. F., aged 27, was first seen on Nov. 22, 1944, at which time he stated that his left eye had felt irritated for the past several days. Later, he admitted that he had had a positive Wassermann reaction in 1935 and that his mother's Wassermann reaction was also positive. At that time he had received antisyphilitic treatment, and in 1941 he received another course of therapy. During the past year he received intensive antisyphilitic treatment for four months, while in the army. His Wassermann reaction was still positive, with a titer of 6.3, and the right upper central incisor was pegged.

Vision was 20/15 — 1 in the right eye and 20/20 — 1 in the left eye. The right eye was quiet and appeared normal. There was some ciliary injection of the left eye, with deep infiltration of the cornea above. Dense vascularization had already begun.

On examination with the slit lamp, the right eye appeared normal except for a few pigment stars, which were considered to be congenital, on the anterior capsule. There was deep infiltration on the upper part of the left cornea, extending almost to the pupillary area, with dense vascularization above. Ophthalmoscopic examination showed the fundi to be normal and the media clear except for interstitial keratitis in the left eye.

The following treatment was prescribed: atropine sulfate, 1 per cent, twice a day, and yellow mercuric oxide ointment, 1 per cent, twice a day, with massage.

The patient was seen six days later; the infiltration and vascularization had extended well into the pupillary area. Vision was reduced to 20/66. From November 29 to December 6, he was given seven subconjunctival injections of 0.5 cc. of sodium penicillin (1,000 Oxford units of penicillin per cubic centimeter). The injections were given above the cornea, at a point corresponding to the area of vascularization. On the fourth day there was less vascularization. On the eighth day the vascularization appeared about the same as at the last examination.

When the patient was seen on December 21, on the twenty-third day after the first subconjunctival injection of penicillin had been given, the eye appeared quiet, with no ciliary injection. The vascularization was subsiding, and the cornea was clearer.

When he was next seen, on Jan. 11, 1945, on the forty-fourth day, the eye was quiet. The vascularization had completely cleared, but there were some scattered areas of deep infiltration of the cornea.

He was last seen Feb. 15, 1945, three months after the onset of his symptoms. His eye was quiet. There were a few faint opacities scattered over the cornea. Vision was 20/15; his eye otherwise appeared normal.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

OPHTHALMODYNAMOMETRY

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The physiology of the vascular circulation in the human eye is of fundamental importance to the whole of ophthalmology, and, because the behavior of the normal and abnormal phenomena are observable within limits, certain analogies, rightly or wrongly, have been drawn with regard to vascular physiology and its alterations elsewhere in the body. Ophthalmodynamometry, a subject of peculiar interest to many workers in this field, appears to deserve review sequential to 1926, when Duke-Elder [1] so aptly observed:

> The unwieldy literature that has accumulated upon the subject is swollen with wearisomely protracted and often acrimonious discussions of unnecessary hypotheses, with defective and confused experiments based on unsound physiological reasoning, with a multitude of theorizings and a paucity of facts.

REVIEW OF LITERATURE

Vascular Pulsations.—The basic modifying factor of intraocular pressure has been responsible during approximately two generations for the continuing controversy with regard to the essential principles involved, ever since pulsations of the retinal vessels first were observed ophthalmoscopically in the living human eye by Coccius,[2] in 1853. He noted the existence of a venous pulse, as did van Trigt [3] independently in the same year. Duke-Elder,[1] in discussing the occurrence of the venous pulse and the variations of its amplitude, expressed the belief that its incidence and excursiveness are appreciably influenced by the ease of egress of the venous blood and that this is so because pulsation implies the displacement of fluid.

Türk [4] demonstrated that the circulatory system in the eye reacts to variations in pressure more after the manner of a series of rigid tubes than does the circulatory system elsewhere. He stated the belief that this was due largely to the influence of the incompressible ocular contents enclosed under pressure or tension by the partially elastic sclera. Duke-Elder [5] demonstrated experimentally that the intraocular tension is limitedly influenced by the height of the general arterial pressure. The former represents a tissue pressure of 20 to 25 mm. of mercury (Friedenwald,[6] Duke-Elder [7]), rather than the pressure of 1 to 2 mm. of mercury that has been shown to exist elsewhere in the body.

No absolutely accurate method of determining capillary pressure in the eye has been developed, but, with the use of a micropipet, Duke-Elder [1] found experimentally that the pressure in the retinal venous capillaries is approximately 2 mm. of mercury higher than the tissue pressure (intraocular tension) of the eye. He estimated that the pressure in the arteriolar limbs of the retinal capillaries normally was about 50 to 55 mm. of mercury, since he transposed Landis' [8] measurements of pressure in the skin to arrive at a comparable pressure in the eye; that is, Landis demonstrated by the use of a micropipet that, with wide variations, the average pressure in the arteriolar limb of a capillary in the skin was about 30 mm. of mercury. Duke-Elder,[5] in effect, merely added this approximate figure to the combined values of the normal intraocular tension and the retinal venous capillary pressure.

Duke-Elder [1] also has shown that the pressure in the ophthalmic artery is only slightly below the

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1. Duke-Elder, W. S.: The Ocular Circulation: Its Normal Pressure Relationships and Their Physiological Significance, Brit. J. Ophth. **10**:513-572 (Oct.) 1926.

2. Coccius, E. A.: Ueber die Anwendung des Augen-Spiegels nebst Angabe eines neuen Instrumentes, Leipzig, I. Müller, 1853.

3. van Trigt, A. C.: Der Augenspiegel, seine Anwendung und Modificationen, nebst Beiträgen zur Diagnostik innerer Augenkrankheiten, Lahr, J. H. Geiger, 1854.

4. Türk, S.: Untersuchungen über die Entstehung des physiologischen Netzhautvenenpulses, Arch. f. Ophth. **48**:513-557, 1899.

5. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1.

6. Friedenwald, J. S.: The Pathology of the Ocular Changes in Nephritis and Hypertension, in The Kidney in Health and Disease, Philadelphia, Lea & Febiger, 1935, pp. 638-664.

7. Duke-Elder, footnotes 1 and 5.

8. Landis, E. M.: Micro-Injection Studies of Capillary Blood Pressure in Human Skin, Heart **15**:209-228 (May) 1930.

level of the systemic, brachial arterial pressure in the normal person but that the former is approximately 25 per cent greater than the arterial pressure entering the eye. The latter varies from 65 to 85 mm. of mercury. The gradient of pressure fall from the central retinal artery, however, is somewhat less than that in other organs, since the capillary pressure in the eye is higher, barring the effects of gravity, than it is elsewhere. It is probable that in the eye the greater part of this fall occurs on the arterial side of the capillary bed, and, as this author pointed out, considerations with regard to the dialysate origin of the aqueous fluid suggest that it does so.

There always exists a pulse in all of the arterial vessels of the body, and this extends down the arterial system with progressively decreasing amplitude. The pulse in the intraocular arterial channels apparently does not differ from that elsewhere in the body except that the intraocular pressure mechanically alters it. The latter varies directly with the blood pressure in the capillaries, and the penetration into the capillary circulation of the variations of the systemic pressure is determined by the height of the general arterial pressure. Complete obliteration of the arteries in the eye may occur at diastole if the diastolic pressure, at the moment, is less than the intraocular pressure. The veins will be full in the eye thus under observation and, therefore, under a pressure higher than that of the intraocular pressure. The capillary pressure must be still higher than the venous pressure, however, since circulatory activity continues indefinitely; thus, capillary pressure may become higher than the diastolic pressure within the entering arteries. Duke-Elder [5] stated, however, that: ". . . in normal circumstances the capillary pressure is less than the diastolic, but it need not be, it often is not. . . ."

The occurrence of a pulse in the retinal artery first was noted by von Jäger [9] in 1854, but that a spontaneous pulse occurs in the retinas of normal eyes first was observed by Donders [10] in 1855, shortly after the introduction of the ophthalmoscope. Becker,[11] in 1872, expressed agreement with Donders' findings, and Ballantyne,[12] in 1913, estimated that it will be encountered in approximately 36 per cent of all normal persons and that it may be accompanied with movement of the retinal arterial vessels themselves. The amplitude of the pulse, especially in the branches of the larger vessels, usually may be observed only with special methods because normally it is so small. De Speyr,[13] in 1914, however, demonstrated that physiologic excursions of the pulse too slight to be seen with the standard ophthalmoscope could be observed almost constantly in normal persons with the Gullstrand ophthalmoscope. This observation was confirmed by Kümmell [14] in 1915. Galezowski,[15] in 1916, noted the occurrence of an arterial pulse in the choroid, and Onishi,[16] in 1913, expressed his opinion that it could be discerned entoptoscopically in the capillaries. This was confirmed by Scheerer [17] and Fortin [18] independently. Fortin,[18] Bailliart,[19] Fritz [20] and others stated the belief that capillary entoptoscopic phenomena and their proper interpretation are important diagnostic aids in the clinical differentiation of the various forms and stages of local and diffuse vascular diseases. This has yet to receive widespread confirmation.

The degree of excursiveness, or amplitude, of the observable pulsations of the retinal arterial vessels varies considerably both in normal and in disease states. Friedenwald [21] suggested that the pulsations be reconsidered from the standpoint of retinal vascular dynamics with regard to their causation and appearance. He offered the following classification: (1) serpentine, (2) expansile, (3) collapsing and (4) tonic. The first is distinguishable as a movement characterized by a slight shifting of the arterial channel with each cardiac pulse. The displacement may be lateral, or there may be some slight bending or knuckling

9. von Jäger, E.: Ueber die sichtliche Blutewegung im menschlichen Auge, Wien. med. Wchnschr. **4**:36 and 69, 1854.

10. Donders, F. C.: Ueber die sichtbaren Erscheinungen der Blutbewegung im Auge, Arch. f. Ophth. **1**:75-105, 1854-1855.

11. Becker, O.: Ueber die sichtbaren Erscheinungen der Blutbewegung in der menschlichen Netzhaut, Arch. f. Ophth. **18**:206-296, 1872.

12. Ballantyne, A. J.: Pulsation of the Retinal Arteries, Ophthalmoscope **11**:271-285 (May) 1913.

13. de Speyr, T.: Le pouls des artères rétiniennes: Phénomène physiologique, Ann. d'ocul. **152**:419-429 (Dec.) 1914.

14. Kümmell, R.: Ueber Pulserscheinungen der Augengefässe, Arch. f. Augenh. **78**:336-358, 1915.

15. Galezowski, J., cited by Duke-Elder.[1]

16. Onishi, Y.: Ein Fall von solitärtuberkelverdächtiger Veränderung des Augenhintergrundes, Nippon Gankwa Gakukwai Zasshi **18**:320-334, 1913.

17. Scheerer, R.: Die entopische Sichtbarkeit der Blutbewegung im Auge und ihre klinische Bedeutung, Klin. Monatsbl. f. Augenh. **38**:67-107, 1924.

18. Fortin, E. P.: Vision directe dans son propre œil des globules du sang et leurs mouvements; applications a l'étude de l'artèrosclérose, de l'insuffisance aortique du glaucome et des troubles capillaires, Semana méd. **2**:126-129 (July 16) 1925.

19. Bailliart, P.: L'hypertension artérielle rétinienne, Internat. Cong. Ophth. (1937) **1**:87-142, 1938.

20. Fritz, M.: Rapport des pressions sanguines humerales et rétiniennes, Bull. Soc. belge d'opht. **67**:67-75, 1933.

21. Friedenwald, J. S.: Retinal Vascular Dynamics, Am. J. Ophth. **17**:387-395 (May) 1934.

of the vessel. The arterial channel may enlarge during systole and decrease in caliber during diastole; this type he termed expansile. Almost complete emptying during the diastolic shrinkage was termed collapsing. There occasionally are observed in some instances of pregnancy and of arteriolar sclerosis the halting, slow progression down the vessels of a ring or zone of relative constriction; these movements were called tonic.

The incompressible ocular contents communicate the pressure pulse to the elastic sclera, where it becomes a volume pulse. The latter normally is not grossly visible except when it is magnified by the lever of the tonometer. It is accentuated when the distensibility of the sclera pathologically becomes increased. This field of investigation has been reviewed elsewhere (Duke-Elder [1]).

Vascular Manometry.—It is known that the normally small retinal arterial pulsations will become progressively larger when the intraocular pressure is raised.[5] Thus, the eye may be converted into a natural sphygmomanometer by the application of the same familiar principles that are involved in the clinical measurement of the systemic arterial blood pressure with the use of the commonplace Riva-Rocci [22] apparatus. This pulse may be artificially induced and become grossly visible in the normal person by the application of gently increased pressure on the globe. The younger the person, the more extensive is the pulsation produced and the less is the pressure required.

The amplitude of this visible pulse increases as the intraocular pressure is increased, until the arteries are seen to be completely collapsed during a portion of the cardiac cycle, at which point the pulsation is maximal. A continued increase of the intraocular pressure will cause the amplitude of this pulsation to decrease progressively, until the incoming blood flow ceases. The systolic pressure is overcome at this point, with cessation of the pulse and collapse of the arterial vessels. The vessels, in the absence of structural changes, will not be visible under the latter conditions because not only are the walls of the retinal vessels normally transparent but there will now exist a transient tissue anemia. Duke-Elder [5] stated: "The point of maximum pulsation therefore records the diastolic, of cessation of pulsation the systolic pressure."

The application of pressure, whether positive (Bailliart [19] and his followers) or negative (Kukán,[23] Linksz [24]), to the external surface of the globe produces an increase in intraocular pressure, and, the contents of the eye being incompressible, the lumen of the retinal vessels tends to diminish in diameter. The intraocular pressure, under certain artificial or pathologic conditions, may become equal to that of the diastolic blood pressure within the vessels, and the two pressures will neutralize each other. The vessels at this time, then, contain blood under no pressure, and patency is maintained by the structure of their walls. The walls thus being completely relaxed, a maximum distention normally is presented to the oncoming systemic pulse wave, and a correspondingly large excursion of the pulse ensues.

The firmness of the wall of the retinal artery is overcome when the intraocular tension is increased beyond the retinal diastolic pressure. The pulse wave then must expend a portion of its energy in overcoming the increased intraocular pressure on the compressed arterial wall, with the result that the excursions of the pulse wave within this portion of the vessel are less extensive in proportion to the excess of pressure on the outside of the wall of that vessel. The retinal vessels normally sustain an internal pressure approximately equal to that sustained by vessels of a similar order of size elsewhere in the body, but the pressure in the terminal arterioles most probably is somewhat higher than the average elsewhere. The intraocular pressure, however, of approximately 20 mm. of mercury, exerts an external supportive force on the intraocular vessels. Friedenwald [6] stated:

> It is perhaps as a response to this relief from internal strain that the unusual delicacy of the retinal arterial wall is to be understood. This delicacy of structure may explain the unusually great local effects of changes in blood pressure if these local effects are truly disproportionate to those in other organs and not merely more easily recognizable.

The diastolic blood pressure in the central artery of the retina and in its arteriolar branches normally is greater than the intraocular pressure. An arterial pulsation of varying degree is observed with certain systemic and intraocular conditions, such as aortic insufficiency, hyperthyroidism, impending syncope, severe anemias and glaucoma.[25] The pulsation appears due to the tendency toward equalization of the intraocular

22. Riva-Rocci, S.: Un nouvo sfigmomanometro, Gazz. med. di Torino **47**:981, 1891.

23. Kukán, F.: Ergebnisse der Blutdruckmessungen mit einem neuen Ophthalmodynamometer, Ztschr. f. Augenh. **90**:166-191 (Oct.) 1936.

24. Linksz, A.: Improved Model of the Kukán Ophthalmodynamometer, Am. J. Ophth. **25**:705-713 (June) 1942.

25. (*a*) Bailliart, P.: The Retinal Circulation in the Normal and Pathologic State, translated by J. E. Lebensohn, Chicago, Professional Press, Inc., 1928; (*b*) footnote 19. (*c*) Espildora-Luque, C.: L'hypertension artérielle rétinienne solitaire, Internat. Cong. Ophth. (1937) **2**:156-182, 1938. (*d*) Duke-Elder.[5]

pressure and the retinal diastolic blood pressure; for example, in cases of aortic insufficiency with regurgitation the latter undergoes a relative reduction, whereas in cases of glaucoma the former increases.

It is possible to elevate the intraocular pressure by instrumentation, by means of manometry or of ophthalmodynamometry.[1] Duke-Elder [5] stated the belief that the former method yields the only reliable values; Bailliart [19] remains the chief exponent of the latter, which Terson termed tonoscopy and Magitot called sphygmoscopy.[26]

Duke-Elder [1] devised an apparatus by means of which saline solution is forced into the eye after a manometer has been inserted. The pulsatory pressure in the intact eye is elevated by forcible pressure applied externally to that eye while the vascular pulsatory movements are observed ophthalmoscopically. Von Graefe,[28] in 1854, first correlated this vascular activity with alterations in the intraocular and the systemic arterial pressure. He elaborated his thesis in the following year; however, von Schultén,[29] in 1884, was the first to measure the pressure in the central artery of the retina (table 1). He employed dogs as subjects and attempted to correlate his recorded vascular pressures with the deduced and observed reductions in caliber of the retinal vessels brought about by external pressure on the globe.

Bajardi,[30] in 1906, devised a tonometric type of instrument with which he could measure units of

TABLE 1.—*Normal Retinal Arterial Blood Pressures Determined with Methods Other Than That of Bailliart*

Year	Author	Method	Interpreted as Millimeters of Mercury: Diastolic	Systolic
1881	Weiss, O.: Ztschr. f. Augenh. **25**: 1-14, 1881	Manometry (laboratory animal)	50 -70	80 -100
1884	von Schultén [29]	Manometry; tonometry (laboratory animal, central artery of retina)	.....	90 -100
1906	Bajardi [30]	Ophthalmodynamometry (Bajardi)	?	?
1911	Rubino [33]	Ophthalmodynamometry (Bajardi)	49 -59	58 - 67
1914	Henderson [34]	Ophthalmodynamometry (Henderson)	10 -25 *	.....
1917	Bailliart [27a]	Entoptoscopy	40	69
1923	Smith [41]	Manometry (laboratory animal)	40 -50	70 - 90
1924	Seidel, E.: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **44**: 79-86, 1924	Manometry (anterior ciliary artery)	30 -45	55 - 75
1924	Bliedung [31]	Ophthalmodynamometry (Bliedung)	55 -98	96 -165
1924	Lullies, H., and Gulkowitsch, L., cited by Kukán [23]	Manometry (laboratory animal)	54 -70	91 -108
1926	Duke-Elder [1]	Manometry (laboratory animal)	59 -69	83 - 94
1927	Baurmann, M.: Arch. f. Augenh. **118**: 118-130, 1927	Entoptoscopy	40 -68	.....
1930	Baurmann [48]	Ophthalmodynamometry (Baurmann)	36	.....
1934	Spinelli [49]	Ophthalmodynamometry (Spinelli)	36 -48	.....
1934	Uyemura and Suganuma [50]	Ophthalmodynamometry (Uyemura and Suganuma)	36.4	56.5
1936	Suganuma [52]	Ophthalmodynamometry (Uyemura and Suganuma)	30.6-54.8	50.2- 85.5
1936	Sobánski [47]	Ophthalmodynamometry (Sobánski)	45	75
1936	Kukán [23]	Ophthalmodynamometry (Kukán)	42.3	.....
1937	Keil [51]	Ophthalmodynamometry (Keil)	35 -40	65 - 75
1937	Müller, Brüning and Sohr [46]	Ophthalmodynamometry (Bailliart, Sobánski and Uyemura and Suganuma), eyes of cadavers in situ	36 -48	.....
1941	Linksz [59]	Ophthalmodynamometry (Linksz)	39 -46.5	65 - 75
1943	Gutmann [52]	Ophthalmodynamometry (Gutmann), rabbits	40.3-49.5	59 - 62.1

* Values for tonometric readings must be added to these figures in individual cases.

behavior of the retinal vessels thus can be observed microscopically by the excursions of an air bubble in a capillary tube, and this activity is correlated with the volume pulse of the globe, its amplitude and the points of maximum oscillation and the cessation of oscillation of the arterial pulse. This method is not adapted to practical clinical use.

The second method, that of Bailliart,[27] is a procedure by means of which the intraocular pressure applied to the external surface of the living human eye. No records of the figures he obtained are available, although Bliedung [31] and Cattaneo [32] referred to them. Rubino,[33] in 1911,

26. Bailliart, P.: Ophthalmodynamometry, in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940, pp. 195-199.

27. Bailliart, P.: (*a*) Circulation artérielle rétinienne: Essais de détermination de la tension artérielle dans les branches de l'artère centrale de la rétine, Ann. d'ocul. **154**:257-271, 1917; (*b*) La circulation rétinienne à l'état normal et à l'état pathologique: Procédés modernes d'examen et de diagnostic, Paris, Gaston Doin, 1923.

28. von Graefe, A.: Notiz über die Pulsphänomene auf der Netzhaut, Arch. f. Ophth. **1**(pt. 1):382-390, 1854.

29. von Schultén, M. W.: Experimentelle Untersuchungen über die Circulationsverhältnisse des Auges, Arch. f. Ophth. **30**(pt. 3):1-76, 1884.

30. Bajardi, G., cited by Rubino.[33]

31. Bliedung, C.: Die Beziehungen zwischen allgemeinem Blutdruck, Blutdruck in den intraokularen Gefässen und Augendruck, Arch. f. Augenh. **94**:198-257, 1924.

32. Cattaneo, D.: PAR (Pressione dell'arteria centralle della retina) e alterazioni retiniche nelle encefalopatie a focolaio da disturbi circolatori, Internat. Cong. Ophth. (1937) **2**:112-119, 1938.

33. Rubino, C.: La pressione del sangue nell'arteria retinica e suoi rapporti con la pressione nel circolo del Willis, Riforma med. **27**:1345-1353 (Dec. 4) 1911.

published the values obtained by him with the Bajardi apparatus. Henderson,[34] in 1914, devised a small, ingenious hand apparatus for the measurement or estimation of retinal arterial pulsation. He utilized a Geneva lens measure graduated, apparently more or less arbitrarily, in millimeters of mercury, instead of in diopters. The pointed foot plate was replaced with a small knob. He expressed the belief that his instrument would register in millimeters of mercury the pressure which when exerted on the globe through the eyelid was sufficient to bring about the appearance of the diastolic pulsation. Magitot[35] stated that the value for the intraocular pressure was added to the figure obtained for the diastolic retinal blood pressure; Henderson's original communication, however, makes no mention of specific values for intraocular pressure other than to state that the retinal diastolic blood pressure ranged in children from 10 to 15 mm. of mercury higher than the intraocular tension and in adults from 15 to 25 mm. higher.

Bailliart[36] previously, in 1909, had observed that rather strong digital pressure on the globe was required to bring about the disappearance (systolic pressure) of the retinal arterial pulse in patients with elevated systemic blood pressure. He stated the belief that this was of clinical significance. Black,[37] in 1911 and Deyl,[38] in 1912, confirmed this observation and tended to agree with the derived conclusions.

Bailliart,[39] in 1917, recalling Marey's "law" of the inverse relationship between heart rate and arterial pressure, and employing the mechanical principles of the Bloch-Verdin[40] sphygmomanometer, devised a standardized tension spring instrument for applying and registering increasing pressures on the living human eye. Priestly Smith[41] stated that Bailliart had no previous knowledge of Henderson's apparatus. A Schiøtz tonometer (old model) then was used to determine the intraocular tensions (or pressures) for correlation with the retinal diastolic and systolic blood pressures obtained. Bailliart termed the apparatus an ophthalmodynamometer, and two types were manufactured. Each essentially is a cylinder arrangement, but one model has etched on the piston or rod a column of horizontal graduated markings. The rod slides upward and downward within the cylinder or sleeve of the instrument and works against a spring. The other model possesses a dial with radial markings on its periphery. A pointer which is activated by the movements of the piston within the metal sleeve is directed to these markings; a second pointer registers the highest reading obtained. Both instruments are calibrated to measure retinal diastolic and systolic blood pressures ranging from 10 to 150 Gm. of water in units of 10.

Pressure may be made on the eye with an ophthalmodynamometer during an ophthalmoscopic examination after local anesthetization has been induced. The retinal blood pressure values obtained may be read from the scale incorporated in the instrument, although it is necessary to convert these figures into units of millimeters of mercury, when the intraocular tension is known, for comparison and correlation with the systemic brachial blood pressures. The conversion graph of Magitot and Bailliart,[42] which is based on values obtained from studies on cat eyes, is used for this purpose with this instrument. Duke-Elder[1] has pointed out that the method of Bailliart involves several fallacies in principle and that it is not the pressure in the branches of the central artery of the retina, but the pressure in the ophthalmic artery, that is obtained. The maintenance of a uniform pressure normally, without subjective fluctuations in the ophthalmic artery, is believed to be effected because of the very appreciable reduction in caliber of the internal carotid artery immediately distal to the branching off of the ophthalmic artery.[21]

Numerous workers have recorded their observations with the ophthalmodynamometer of Bailliart; while many of the values are relatively low, some of the figures vary from others by more than 100 per cent. There also are recorded

34. Henderson, T.: Clinical Proof of the Venous Level of the Intra-Ocular Pressure and a Method of Estimating the Arterial Diastolic Pressure in the Eye and Its Clinical Significance, Tr. Ophth. Soc. U. Kingdom **34**:309-315, 1914.

35. Magitot, A. P.: How to Know the Blood Pressure in the Vessels of the Retina, Am. J. Ophth. **5**:777-784 (Oct.) 1922.

36. Bailliart, P.: Contribution à l'étude du pouls rétinien, Clin. opht. **15**:178-183, 1909.

37. Black, M.: An Index to the General Blood Pressure: The Venous Pulse and Blanching of the Retinal Vessels Induced by Pressure on the Eyeball, J. A. M. A. **57**:362-363 (July 29) 1911.

38. Deyl, A.: Retinale Angiosklerose als differential diagnostiches Symptom, Wien klin. Wchnschr. **26**:33-51, 1912.

39. Bailliart, P.: (*a*) La pression artérielle dans les branches de l'artère centrale de la rétine; nouvelle technique pour la déterminer, Ann. d'ocul. **154**:648-666, 1917; (*b*) footnote 27.*a*

40. Bloch, A. M.: Note sur un perfectionnement apporté a mon sphygmomètre, Compt. rend. Soc. de biol. **48**:745-746 (July) 1896.

41. Smith, P.: The Blood Pressure in the Eye and Its Relation to Chamber Pressure, Brit. J. Ophth. **7**:449-469 (Oct.) 1923.

42. Magitot, A. P., and Bailliart, P.: Modifications de la tension oculaire sous l'influence de pressions exercées sur le globe (recherches expérimentales), Ann. d'ocul. **156**:656-666, 1919.

variations in figures obtained on different occasions by the same authors using the same technic. Thus, Bailliart [39a] in 1917 obtained average values of 25 to 30 and 50 to 70 mm. of mercury for the normal retinal diastolic and systolic blood pressures, respectively, in man, and Magitot and Bailliart [43] in 1921 determined the normal range in man to be 30 to 35 and 70 to 80 mm. of mercury for these two blood pressures. The same authors in 1919 had obtained values as high as 100 to 130 mm. of mercury for the retinal diastolic blood pressure in the cat and in the dog, respectively.[42] Bliedung,[31] as well as Fritz,[20] and Constantine [44] have recorded the widest range of values for the retinal systolic blood pressure. Bliedung,[31] who used his own device, also found the widest range of recorded retinal diastolic blood pressures. Workers recording narrow ranges (table 2) are in the majority, however, although less striking variations, with the exception of those just mentioned, exist with regard to the figures obtained by workers with methods other than the technic of Bailliart (table 1). It is of interest to note that Lebensohn,[45] who, in 1925, was the first in this country to record his observations with the ophthalmodynamometer of Bailliart, obtained readings that closely approximate those of most other workers.

Constantine,[44] in her study of the interrelationship of retinal and systemic arterial blood pressures and tonometric pressure in normal and in syphilitic patients, stated: "The method [of Bailliart] is palpably . . . inaccurate and open to wide differences, depending on the personal equation of the observer." Bailliart felt that certain errors could be eliminated to some extent by furnishing both types of his instrument with a convex rather than a concave foot plate, since if it were equipped with the latter the examiner would have difficulty in ascertaining whether or not a portion of the edge of the foot plate or the whole of the concave disk was exerting pressure on the sclera. He expressed the opinion that some possible errors, therefore, would be decreased if only a convex surface were permitted for application to the eye. This view has been disputed by the findings of Müller, Brüning and Sohr,[46] who, using their reduction scale (or conversion graph) reading in millimeters of mercury, rather than in grams of water, and working on the human eye and the cat's eye, found no differences in the values obtained with the apparatus of Bailliart [27a] and that of Sobánski.[47] The latter has a concave foot plate.

TABLE 2.—*Retinal Arterial Blood Pressures in Normal Persons Determined with Ophthalmodynamometric Method of Bailliart*

Year	Author	Interpreted as Millimeters of Mercury	
		Diastolic	Systolic
1917	Bailliart* [27a]	67	98
1917	Bailliart [39a]	25 -30	50- 70
1920	Velter, E.: Arch. d'ophth. **37**: 88-94, 1920	35	60- 65
1920	Duverger, C., and Barré, J. A.: Arch. d'opht. **37**: 71-87, 1920	50 -60	80-100
1921	Magitot and Bailliart [43]	30 -35	70- 80
1921	Vossius, A.: Arch. f. Ophth. **104**: 320-324, 1921	.....	70
1921	Gaudissart, P.: Am. J. Ophth. **4**: 500-502 (July) 1921	30 -35	70- 80
1922	Salvati, G.: Ann. d'ocul. **159**: 69-71, 1922	32 -50	60- 70
1925	Stasinski, J.: Klin. oczna **3**: 49-58, 1925	30 -35	67- 70
1925	Lebensohn [45]	30 -35	65- 75
1925	Vita, A.: Ann. di ottal. e clin. oculi. **53**: 904-913, 1925	30 -35	70- 75
1925	Verway, A.: South African M. Rec. **23**: 427-429, 1925	Equals radial pressure	
1925	Monjukova, N., and Pletneva, N.: Arch. oftal **1**: 212-242, 1925	35	70
1926	Baurmann, M.: Klin. Monatsbl. f. Augenh. **41**: 874, 1926	49.7-54.9	.....
1926	Rasvan, N.: Bull. Soc. roumaine d'opht., 1926, pp. 201-205	30 -35	65- 70
1926	Lida, E., and Adrogué, E.: Compt. rend. Soc. de biol. **95**: 1160-1161, 1926	40 -50	80-100
1926	Samojloff, A. J.: Ann. d'ocul. **163**: 689-694 (Sept.) 1926	35	80- 85
1927	Schiøtz, L.: Acta ophth. **5**: 293-297, 1927	50 -56	70- 80
1927	Abramowicz, I.: Klin. oczna **5**: 125-173, 1927	45 -55	70- 90
1927	Kalt, M.: Pression artérielle rétinienne dans l'hypertension intracranienne, Paris, L'expansion scientifique, 1927	35	77
1927	Serr, M.: Arch. f. Ophth. **119**: 6-14, 1927	30 -35	50- 70
1928	Berens, Smith and Cornwall [64]	18 -48	36- 88
1931	Vancea, P.: Arch. f. Opth. **126**: 601-612, 1931	25 -42	58- 77
1932	Guiral [61]	30 -35	70- 80
1933	Fritz [20]	25 -45	60-130
1936	Sobánski, J.: Arch. f. Ophth. **135**: 372-430, 1936	40 -56	68- 88
1937	Bailliart [19]	30 -35	50- 80
1937	Bengisu [58]	23 -55	.....
1939	Constantine [44]	22 -72	65-112
1941	Koch [55]	20 -41	.....

* Includes value of 20 mm. of mercury for normal tonometric readings.

Aside from the more recent modifications and the newer, ingenious ophthalmodynamometric instruments of Baurmann,[48] Spinelli,[49] Uyemura

43. Magitot, A. P., and Bailliart, P.: Recherches sur l'action de vasomoteurs oculaires: Pression comparée dans les vaisseaux de l'iris et de la rétine, J. de physiol. et de path. gén. **19**:532-541, 1921.

44. Constantine, E. F.: A Study of the Interrelationship of Retinal and Systemic Arterial Pressure and Intra-Ocular Tension in Normal and Syphilitic Patients, Am. J. Ophth. **23**:436-445 (April) 1940

45. Lebensohn, J. E.: The Determination of Retinal Blood Pressure, Illinois M. J. **48**:212-214 (Sept.) 1925.

46. Müller, H. K.; Brüning, A., and Sohr, H.: Die Eichung der Dynamometer von Bailliart und Sobánski am menschlichen Leichenauge, Internat. Cong. Ophth. (1937) **4**:44-51, 1938.

47. Sobánski, J.: Ein Ophthalmodynamotonometer und seine Handhabung, Klin. Monatsbl. f. Augenh. **96**:351-356 (March) 1936.

48. Baurmann, M.: Ein neues Dynamometer, Arch. f. Ophth. **124**:693-704, (Aug.) 1930.

49. Spinelli, F.: Angiotensiometro retinico Spinelli, Atti d. Cong. Soc. ital. oftal. (1934), 1935, pp. 795-798.

and Suganuma,[50] Sobánski,[47] Kukán,[23] Keil,[51] Linksz,[24] Gutmann [52] and others, the method and the apparatus used by the majority of the workers in this field have been those of Bailliart (table 2). The published reports of the latter are concerned largely with the clinically diagnostic significance of the blood pressures in the central artery of the retina as measured in its ophthalmoscopically visible branches on the papilla in normal persons and in patients who have diffuse vascular disease with systemic hypertension, whether or not of renal origin.

Duke-Elder [1] determined in the cat with manometric methods that the mean pressure in the ophthalmic artery is about 95 per cent and that in the retinal arterioles about 70 per cent of the mean aortic pressure. Bailliart,[27b] in 1923, with ophthalmodynamometric methods, estimated that the diastolic pressure in the retinal arterioles was about 45 per cent of the diastolic pressure in the brachial arteries of the normal adult.

Magitot and Bailliart [42] previously had found, in 1919, that in eyes with normal intraocular tension a dynamometric pressure of approximately 25 Gm. of water was required to produce the retinal arterial pulse and that 60 to 70 Gm. of water was sufficient pressure to cause its disappearance. Thus, the retinal diastolic blood pressure in normal persons was believed to be 30 to 35 mm. of mercury, while the retinal systolic blood pressure, according to their conversion graph (reduction scale), was 65 to 70 mm. of mercury. The figure for the diastolic pressure was the more constant, and it was found that a factor, 0.45, could be utilized to predict the retinal diastolic blood pressure if the systemic brachial diastolic blood pressure was known. Multiplying the systemic pressure by this factor yielded a theoretic ideal, or normal, value for the retinal diastolic blood pressure.

A similar but not quite so consistent a constant was offered in the factor 0.54, which, when multiplied by the value of the known systemic brachial systolic blood pressure, was believed to yield the value for the normal retinal systolic blood pressure. Bailliart [25a] stated it as his opinion that the latter, at least, was of practical clinical importance in that he deemed it unwise to exert a pressure of more than 150 Gm. of water on the eye, since this represented a pressure less than would be employed by the patient in pressing on his own eye. This pressure is well below that required to produce an oculocardiac reflex. He expressed the belief, too, that the constants, or factors just mentioned, had a further clinical application, since their use could detect deviations from the theoretic normal and not infrequently could be relied on in instances in which it was not feasible to use his apparatus. Thus, if these derived values are greater than 5 to 10 mm. of mercury, there may, he stated, be said to exist a truly disproportionate or abnormal reciprocal relationship between the systemic and the intraocular blood pressure system.

Retinal vascular hypertension and hypotension, Bailliart and his followers [53] asserted, may be diagnostic in very early phases of alteration in the systemic blood pressure, as well as of clinical value when the change in the retinal pressure exists in the "solitary" state. The latter, for example, refers to the existence of a disproportionate reciprocal relationship encountered by these workers in cases of increased intracranial pressure without systemic hypertension; that is, they found the retinal blood pressures to be elevated. They stated, too, that there may occur prodromal retinal hypertension without any change in the ophthalmoscopic findings or in the systemic blood pressure, and they asserted that these circumstances constitute an aid in the diagnosis of diffuse arterial disease with hypertension.

There now exists an extensive literature with regard to the ophthalmodynamometric investigations of ocular and systemic pathologic states in which variations in the retinal blood pressures and in the intraocular tension have been suspected. Many of the published figures, as has been indicated, are inconclusive and controversial; accordingly, no unanimity of interpretation exists. Wagener and Keith,[54] however, in their comprehensive review of diffuse arteriolar disease with hypertension, probably expressed the consensus in the statement:

50. Uyemura, M., and Suganuma, S.: Ueber einen neuen Ophthalmodynamometer, Acta Soc. ophth. jap. **38**:1835-1844, 1934.

51. Keil, J.: Ein neues Ophthalmodynamometer, Klin. Monatsbl. f. Augenh. **99**:625-636 (Dec.) 1937.

52. Gutmann, A.: Pressure in Central Artery of Retina in Allergy with Description of a New Ophthalmodynamometer, Arch. Ophth. **29**:457-460 (March) 1943.

53. (*a*) Bailliart, P.; Magniel, and Saragea: Mesures de la pression artérielle rétinienne et de la tension céphalo-rachidienne dans quelques cas d'hypertension artérielle, Arch. d. mal. du cœur **17**:289-294 (May) 1924. (*b*) Bailliart.[19] (*c*) Espildora-Luque.[25c] (*d*) D'Osvaldo, E.: Sull'importanza clinica del segno di Bailliart come indice di ipertensione arteriose cefalica (Espildora), Lettura oftal. **10**:455-466 (Oct.) 1933. (*e*) Suganuma, S.: Studien über den Blutdruck in der Zentralarterie der Netzhaut: II. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei verschiedenen Formen von allgemeiner Hypertonie und über die sog. isolierte zephale Hypertension, Klin. Monatsbl. f. Augenh. **97**:498-514 (Oct.) 1936.

54. Wagener, H. P., and Keith, N. M.: Diffuse Arteriolar Disease with Hypertension and the Associated Retinal Lesions, Medicine **18**:317-430 (Sept.) 1939.

The pressures as measured by this method may be lower than the actual figures, but they furnish a ready and probably fairly reliable method of determining variations from the normal in pathologic states.

My own investigations tend only partially to confirm this point of view.[55]

CLINICAL EVALUATION

It is impossible accurately to evaluate for clinical comparison the results obtained with the ophthalmodynamometer by many of the workers in this field not only because dissimilar instruments and technics have been employed but because the majority of the investigators (as has been true, also, in the study of vascular micrometry) have not troubled sufficiently to correlate the values obtained with reference to classification of the disease groups studied, age subgroupings, systemic blood pressures, ophthalmoscopic findings and other diagnostic minutiae. It appears, too, that not infrequently there has been inadequate comprehension of vascular physiology in general. Conclusions have been derived in many instances in which there was little recognition of the existence of errors in measurements due, most unfortunately, to the intangible factor inherent in the personal equation necessarily present on the part of the observer in any clinical examination. Tuyl,[56] in particular, stated that only comparative values, at best, are obtainable with the ophthalmodynamometric technic and that long experience and numerous readings in every case are necessary in order to arrive at acceptable values. It is of interest that the proponents of vascular dynamometry enthusiastically believe it elicits clinical information of at least somewhat, if not appreciably, greater value than any other single test or procedure for the recognition and differential diagnosis of many abnormal and pathologic states, of either general or local ocular origin.

Despite the many contributions in the field of ocular dynamometry, there are tremendous variations in the values obtained for normal retinal blood pressures no matter with what instrument the examinations were conducted (tables 1 and 2). It is impossible to denote any single exact value for either the diastolic or the systolic blood pressure, although many workers have concluded that there must be some such figure. It appears unreasonable, therefore, to suppose that any single value for the retinal blood pressures can be given when it is known that no single value can be cited with reference to the systemic blood pressures no matter in what location or with what apparatus they are determined.

The values for the normal retinal diastolic blood pressure, obtained through more than two decades of investigation with the ophthalmodynamometer of Bailliart, range from a low of 18 to a high of 72 mm. of mercury, and there is some overlapping with the values for the retinal systolic pressure, since the range for the latter is 36 to 130 mm. of mercury (table 2). Similar variations in the range of retinal blood pressures have been obtained when instruments and methods other than Bailliart's have been employed; however, the ranges with manometric devices, although not clinically practical, generally have been narrower than when some form of the dynamometer has been used (table 1).

Retinal capillary pressures also have been studied by several workers, whose contributions have been reviewed by Kukán.[23] Fortin,[18] Bailliart,[19] Fritz,[20] Baratta[57] and others tended to attribute greater physiologic importance than had heretofore been thought necessary to the role played by these smaller vascular channels in systemic hypertensive disease, as well as in states of altered intracranial and intraocular function. Numerous objective and subjective procedures have been devised or suggested whereby the physiologic and the abnormally physiologic status of these vessels might be employed as clinical aids, particularly in cases of hypertensive disease. None appear to be satisfactory.

In general, ophthalmodynamometric values for retinal diastolic blood pressures, in millimeters of mercury, probably must be considered normal if the value obtained does not exceed 55.[55] The lower limit of normal is similarly variable and somewhat more difficult to determine. Bengisu[58] probably represents the consensus in his values for the normal retinal diastolic blood pressure obtained with the dynamometer of Bailliart. His examinations indicated that approximately 10 per cent of normal persons will have a retinal diastolic blood pressure of 23 to 25 mm. of mercury, that a second group, representing 45 per cent of normal persons, will have values ranging from 35 to 45 mm. and that a third, more elderly, group, of 45 per cent of normal persons, will

55. Koch, F. L. P.: Retina in Systemic Vascular Hypertension: A Clinical Study of the Caliber of the Retinal Arterioles and the Retinal Arterial Diastolic Blood Pressure, Arch. Ophth. **26**:565-581 (Oct.) 1941.

56. Tuyl, A., in discussion on Espildora-Luque.[25c]

57. Baratta, O.: Studio sulla circolazione vascolare della retina con particolare riguardo al comportamento della pressione dell'arteria centrale (PAR) e dei capillari della macula (PCR) nelle affezioni renali, Ateneo parmense **9**:265-295 (July-Aug.) 1937.

58. Bengisu, N., in discussion on Lobeck, E.: Ueber die ophthalmoskopische Messung der Durchmesser der Netzhautgefässe und ihre allgemein klinische Bedeutung für die Differentialdiagnose bei Hochdruck- und Nierenkrankheiten, Internat. Cong. Ophth. (1937) **2**:262-164, 1938.

have values of from 50 to 55 mm. of mercury. Linksz,[59] with his negative pressure dynamometer, found slightly higher values: 39 mm. of mercury for persons from 15 to 30 years of age, 44.5 mm. for persons from 30 to 50 years of age and 46.5 mm. for persons from 50 to 70 years of age. My own figures, obtained with the Bailliart device, were somewhat lower.[55]

I found that my values, when expressed, as seems clinically rational, in terms of the percentage ratio of retinal to brachial diastolic blood pressure, ranged from 25 to 51, with means of 36, 40 and 43 per cent for the normal patients in three major age subgroupings, respectively, of 8 to 15, 16 to 40 and 41 to 60 years; however, there was considerable overlapping from one individual to another. There existed a progressive increase in the retinal diastolic blood pressure and in the percentage ratio of the retinal diastolic to the brachial diastolic blood pressure in hypertensive groups. This was less manifest in the patients with chronic glomerulonephritis. The study indicated, however, that a mean percentage ratio that was considered normal, of 55, as has been mentioned, arbitrarily could be established as the upper limit of normal and that, although there was some overlapping of the ratios for patients with mild hypertension in the younger age group with the ratios for normal persons in all age groups and with those for patients with chronic glomerulonephritis, this overlapping was in accord with the fluctuation in systemic blood pressures that is known to exist normally.[55]

Most of the workers with the Bailliart ophthalmodynamometer have stated, however, that it is difficult to fix an exact value for the minimal or theoretically normal diastolic retinal blood pressure unless the figure for the systemic diastolic blood pressure is multiplied by the factor 0.45. This figure was stated originally by Bailliart to represent the percentage ratio of the normal retinal to the normal systemic diastolic blood pressure. Bailliart [60] expressed the opinion that a comparison of this derived figure with the actual value obtained by the ophthalmodynamometric examination is of diagnostic value when there is a variation of more than 5 to 10 mm. of mercury and that there exists, therefore, a local retinal or cephalic ("solitary") vascular hypertension which a general examination will reveal to be systemic or cerebral in origin. The values obtained in my studies with reference to the theoretic, or derived, as compared with the actual retinal diastolic blood pressures, expressed in millimeters of mercury, and their relationship to the percentage ratios of the retinal and the systemic diastolic pressures indicate that there exist relatively normal values for the nonhypertensive patients but that elevated, abnormal, relatively disproportionate values are found for the hypertensive groups.[55]

Bailliart, Magniel and Saragea [53a] found somewhat similar progressively increasing values for 22 hypertensive patients. These patients were not specifically classified as to the stage of the disease. The systemic diastolic blood pressures in this group ranged from 50 to 180 mm. of mercury, while the retinal diastolic blood pressures ranged from 20 to 120 mm. The percentage ratios varied from 33 to 96, while the spinal fluid pressures ranged from 75 to 320 mm. of water. Guiral,[61] Fritz [20] and other followers of Bailliart generally expressed agreement with these conclusions. In general, a rise in the estimated retinal diastolic blood pressure, in millimeters of mercury, is only roughly proportionate to the rise in brachial diastolic blood pressure. The mean percentage ratio, while it increases as the hypertensive disease becomes advanced, exhibits only a rather narrow range of values from the normal subjects to group 4 (malignant hypertension); however, this ratio is almost directly proportional to that obtained by multiplying the mean brachial diastolic blood pressure for each group of patients by the factor 0.45.

The dynamometer of Uyemura and Suganuma,[50] instead of registering values by means of spring tension, as do most others, depends on hydrostatic pressure. Suganuma [62] measured the retinal diastolic pressure in a single eye, usually the right, of 65 patients with normal blood pressure. These patients ranged in age from 12 to 65 years. Their retinal diastolic blood pressures ranged from 30.6 to 54.8 mm., while the brachial diastolic blood pressure ranged from 42 to 87 mm., of mercury. Intraocular tension with the old model Schiøtz tonometer ranged from 8 to 22 mm. of mercury. Suganuma also obtained dynamometric readings for both eyes of 18 patients, who ranged in age from 16 to 30 years. They were unselected normal persons of both sexes. The mean retinal diastolic blood pressure was 38.08 mm. of mercury, on a basis of values

59. Linksz, A.: A New Instrument for Ophthalmodynamometry, read at the meeting of the New York Society for Clinical Ophthalmology, Nov. 3, 1941.

60. Bailliart (footnotes 25[a] and 27[b]).

61. Guiral, R. J.: La disociación tensional retinohumeral, Arch. de neuro-biol. **12**:275-294 (May-June) 1932.

62. Suganuma, S.: Studien über den Blutdruck in der Zentralarterie der Netzhaut: I. Ueber den Blutdruck in der Zentralarterie der Netzhaut bei gesunden Menschen und über seine Beziehung zum allgemeinen Blutdruck, Klin. Monatsbl. f. Augenh. **96**:74-84 (Jan.) 1936.

ranging from 30.6 to 45.2 mm. of mercury. Since he obtained a mean value of 31 mm. from the readings on single eyes in a similar, but larger, group, the significance of this difference in values is uncertain (table 3).

An analysis of the values obtained by Suganuma was made with reference to age subgroupings, systemic and retinal vascular pressures, the ratio of these pressures in percentages and the theoretic mean ratio obtained by means of the factor, 0.45, of Bailliart. These data are summarized in table 3; in general, it was found that his values for the retinal diastolic blood pressure in normal persons from 8 to 65 years of age are higher than those obtained in my study.[55] The

TABLE 3.—*Analysis of Values Obtained by Suganuma* [62] *in Normal Persons*

Age in Years, Inclusive	Number of Subjects	Mean: Diastolic Blood Pressures, Mm. Brachial	Mean: Diastolic Blood Pressures, Mm. Retinal	Mean: Ratio of Retinal to Brachial Blood Pressure, Per Cent	Theoretic Ratio (Bailliart)
8-15	2 (2 eyes)	57	40	70	26
16-40	58 (58 eyes)	69	38	55	31
41-60 (1 patient of 65)	7 (7 eyes)	65	43	65	29
Mean: all persons.....		69	39	56	31

percentage ratios necessarily are rather higher, too, because of his relatively lower figures for the brachial diastolic blood pressure. This low pressure also results in a somewhat lower theoretic, or ideal, retinal diastolic blood pressure.

Müller, Brüning and Sohr [46] evolved comparative curves for use with the dynamometers of Bailliart, Sobánski and Uyemura and Suganuma. They determined the mean retinal diastolic blood pressure to be 48 mm. of mercury for 180 eyes of 98 persons who probably had been healthy prior to death. These eyes were examined in situ in cadavers a few to twenty-four hours after death in each instance. The Franck manometer was used in conjunction with their investigations. They came to the conclusion that the conversion graph curves of Sobánski and of Bailliart were essentially similar and could be used more or less interchangeably but that attempts to convert the values obtained with the Uyemura-Suganuma instrument in terms of the conversion graphs of the previously mentioned authors would result in a mean value of 60 mm. of mercury for the "normal" retinal diastolic blood pressure. It will be recalled that Duke-Elder,[5] with manometric methods, found that the retinal diastolic blood pressure ranged from 59 to 69 mm. of mercury.

It is interesting to compare the mean values for local ocular and systemic pressures obtained for normal persons by Bliedung,[31] in 1924, by means of a cambric bandage and a hydrostatic device in conjunction with ocular manometry. His figures (table 4) are all very high for the 350 eyes of the 292 patients examined. Their ages ranged from 9 to 67 years, inclusive. The intraocular tension averaged 20 mm. of mercury for the entire group, but the retinal diastolic blood pressures, arterial and arteriolar, were nearly equal to and greater than, respectively, the brachial diastolic blood pressure, expressed in millimeters of mercury. There was a slight increase in the retinal pressures in the older age groups as compared with those in the younger subgroups. Bliedung's values have not been accepted by other workers in this field.

Suganuma,[63] using the dynamometer bearing his and Uyemura's name, determined the ophthalmodynamometric relationships with reference to the systemic blood pressures in normally pregnant women and in women with toxemia of pregnancy. He also obtained what he believed were diagnostic values for patients with hypertensive disease and for patients with "solitary," cephalic hypertension.[53e] This investigator obtained what he considered were normal values in

TABLE 4.—*Intraocular Pressures in Normal Persons (Bliedung* [31]*)*

Grouping: Age Groups, Years	Grouping: Number of Subjects	Grouping: Number of Eyes	Mean: Brachial Diastolic Blood Pressure, Mm. Hg	Mean: Retinal Diastolic Blood Pressure in Central Artery, Mm. Hg	Mean: Diastolic Blood Pressure in Retinal Arterioles, Mm. of Hg	Mean: Intraocular Pressure (Schiøtz Tonometer, Old Model), Mm.
9-15	48	60	63	64	77	22
16-20	48	60	69	71	78	21
21-25	41	50	75	70	81	20
26-35	41	50	69	68	83	21
36-45	44	50	73	70	83	20
46-55	43	50	78	74	87	18
56-67	27	30	84	75	91	18
9-67	292	350	69	69	82	20

normally pregnant women both before and after delivery; however, he studied only 10 patients, 1 of whom he was unable to observe after delivery (table 5). His values for the retinal diastolic blood pressure in this group of patients essentially are the same as those in the normal groups analyzed in table 3. This is true, also, with respect to the systemic diastolic pressures, the percentage ratios and the values for the latter

63. Suganuma, S.: Studien über den Blutdruck in der Zentralarterie der Netzhaut: III. Ueber den Blutdruck in der Netzhautarterie während des Verlaufes der normalen Schwangerschaft und der Schwangerschaftstoxikose, sowie über seine frühdiagnostische Bedeutung, Klin. Monatsbl. f. Augenh. **99**:637-654 (Nov.) 1937.

obtained by means of the Bailliart factor of 0.45. The percentage drop in the brachial diastolic pressure from the value preceding delivery to that following delivery was nearly twice as great as the percentage drop in the retinal diastolic blood pressure, the values being 17 and 10 per cent, respectively.

Suganuma obtained definitely higher, but essentially proportional, values in a similar study on 10 patients presenting various stages of hypertensive toxemia of pregnancy (table 6). It should be noted, however, that the percentage drop from the value preceding delivery to that following delivery was essentially the same in this toxemic group with reference both to their brachial and to their retinal diastolic blood pressures. This is in accord with the findings of Bailliart.[25a]

TABLE 5.—*Analysis of Values Obtained by Suganuma*[63] *for Normally Pregnant Women*

	Values for Ten Patients					
	Before Delivery			After Delivery		
	Arterial Blood Pressures, Mm. of Hg		Intraocular Tension, Mm. of Hg	Arterial Blood Pressures, Mm. of Hg		Intraocular Tension, Mm. of Hg
Age	Systemic	Retinal		Systemic	Retinal	
27	117/78	56.5/36.5	18			
	114/74	58.0/39.4	17	114/68	56.4/36.2	19
26	112/58	59.6/34.0	15			
	104/60	59.6/36.0	16	106/48	58.4/36.0	17
24	120/58	62.6/49.0	15	114/68	59.0/40.2	17
23	112/72	64.2/39.2	15	118/76	63.2/41.8	12
24	112/64	62.6/31.6	13	106/62	59.0/31.2	15
26	89/50	48.0/36.2	10			
	96/55	51.6/34.8	9			
22	112/72	69.4/44.1	13	118/68	58.6/33.8	15
27	118/68	58.3/38.6	15			
	120/70	70.6/48.8	15	116/68	60.4/39.8	17
40	140/96	85.8/54.6	15	124/62	63.1/40.6	15
23	104/48	62.5/39.4	15			
	108/54	72.4/50.2	15	108/56	56.5/36.4	17

Analysis of Mean Values

	Diastolic Blood Pressures, Mm. Hg		Ratio of Retinal to Systemic Diastolic Blood Pressure, Per Cent	Theoretic Ratio (Bailliart) of Retinal to Systemic Diastolic Blood Pressure Multiplied by 0.45
	Systemic	Retinal		
Before delivery	76.95	41.05	53.36	34.62
After delivery	64.00	37.33	58.34	28.80
Decrease, in per cent	17	10		

Suganuma's[53e] studies with respect to other forms of elevation of systemic pressure are summarized in tables 7, 8 and 9. There exists no truly appreciable difference between the values for his various groups of hypertensive patients and the values for various age subgroupings. This is true with respect to all the values obtained and is particularly striking when the mean values for each particular group of hypertensive patients are examined. It also will be observed that the highest recorded mean brachial diastolic blood pressure in his Japanese patients was 116 mm. of mercury. This is of interest, although of doubtful significance, when it is noted that the mean retinal diastolic blood pressures, as well as the percentage ratios, in all these groups generally are as high as, if not higher than, the values for the patients with similar brachial diastolic blood pressures examined in my investigation.[55] The group of patients with toxemia of pregnancy observed by Suganuma had retinal diastolic blood pressures and percentage ratios that approached the lower values obtained in his groups of hypertensive patients.

Bailliart,[26] in his earlier work, as well as later, stated that retinal hypertension might exist independently of sytemic hypertension and that, since the circulation in the retina reflects generally that of the brain, the existence of retinal hypertension thus implies the coexistence of cerebral hypertension, probably largely on the basis of an increased intracranial pressure, whether brought about by local intracranial or by systemic hypertension. Conversely, hypotension also may be encountered. His observations have received

TABLE 6.—*Analysis of Values Obtained by Suganuma*[62] *for Women with Toxemias of Pregnancy*

	Values for Ten Patients					
	Before Delivery			After Delivery		
	Arterial Blood Pressures, Mm. of Hg		Intraocular Tension, Mm. of Hg	Arterial Blood Pressures, Mm. of Hg		Intraocular Tension, Mm. of Hg
Age	Systemic	Retinal		Systemic	Retinal	
21	104/ 80	88.0/64.6	15	114/ 78		
	138/108	.....	..	148/ 98		
	.....	.....	..	142/ 80	84.2/59.8	17
	.....	.....	..	104/ 74	58.6/33.8	17
24	182/102	87.0/65.7	13	118/ 68	60.4/37.6	18
29	130/ 92	80.0/64.2	11	116/ 70	62.1/41.8	13
29	166/108	80.6/65.5	17			
22	110/ 56	60.2/42.8				
	.....	75.4/53.8				
33	166/104	86.8/62.8	16			
	195/134					
	.....	.....	..	168/112	84.0/62.6	13
	.....	.....	..	138/ 95	79.0/55.7	14
30	118/ 76	76.0/48.7	11	122/ 80	85.6/62.2	17
34	186/120	122.7/88.0	21	132/ 88	113.0/84.7	19
25	180/110	82.0/57.1	17	152/ 98	78.5/50.1	19
35	.....	.....	..	200/112	109.0/78.2	

Analysis of Mean Values

	Diastolic Blood Pressures, Mm.		Ratio of Retinal to Systemic Diastolic Blood Pressure, Per Cent	Theoretic Ratio (Bailliart) of Retinal to Systemic Diastolic Blood Pressure Multiplied by 0.45
	Systemic	Retinal		
Before delivery	95.88	62.15	64.78	43.15
After delivery	87.25	57.15	65.50	39.26
Decrease, in per cent	9	8		

support from his followers and from some other investigators.

Guiral,[61] among others, stated the belief that if the retinal vascular pressures were elevated in a patient over 50 years of age there existed imminent danger of a cerebral vascular accident, that if the systemic blood pressure was elevated, although the retinal blood pressure remained high, even greater danger was present but that if the retinal and systemic pressures were proportional the prognosis was less grave. Berens, Smith and Cornwall[64] concluded from their studies on 11 normal persons and on 13 patients with neuro-ophthalmologic syndromes that the method of Bailliart is of value to the trained observer in spite of its inaccuracies but that the use of the ophthalmoscope nevertheless is invaluable. They also stated the opinion that the retinal diastolic blood pressure increases rather markedly as the subject changes from a standing or sitting to a prone position. This view is not altogether in accord with the findings of others, although both Salvati[65] and de Sanctis[66] supported it.

TABLE 7.—*Analysis of Values Obtained by Suganuma*[53e] *for Patients with Essential Hypertension*

Age in Years, Inclusive	Number of Patients	Mean: Diastolic Blood Pressures, Mm.		Mean: Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Brachial	Retinal	
29-39	5 (5 eyes)	109	77	70
41-60 (5 patients 61 to 71)	35 (35 eyes)	106	72	68
Mean: All patients.....		107	73	68

It was the opinion expressed by these authors and by others, particularly Klar,[67] Espildora-Luque[25e] and de Morsier, Monnier and Streiff,[68] that the retinal arterial pressure becomes elevated in the presence of intracranial disturbances, particularly lesions of the posterior fossa, such as neoplasms, trauma and cerebrovascular accidents. The last-mentioned authors asserted that retinal arterial hypertension, nevertheless, is relatively infrequent with tumors, but they agreed with Klar that it is very common as a sequel of cerebral trauma. These workers said that it probably develops subsequent to disturbances of the regulatory centers of the cerebral vasomotor system.

Espildora-Luque,[25e] d'Osvaldo,[53d] Cattaneo,[32] Suganuma[53e] and others examined relatively small groups of patients and concluded that so-called solitary hypertension is present with rather a large number of diseases, both systemic and local, which affect both intracranial and intraocular pressure relationships. Espildora-Luque[25e] has proposed, and Suganuma[53e] is in accord with the suggestion, that this occurrence be termed cephalic arterial hypertension, since it is thought that this rise of retinal vascular pressure occurs in the absence of elevation of systemic blood pressure but in the presence of increased cerebrospinal fluid pressure. These authors and others, on the basis of what appears to be insufficient evidence, stated that this increase of local vascular pressure is coincident with, and secondary to, an increase in blood pressure which is limited to the region of the internal carotid arteries and the circle of Willis and its branches. It is more logical to assume that this increase in local pressure, if it occurs (as seems evident), probably is secondary to the rise of the cerebrospinal fluid, as noted by Pickering[69] in cases of this type. Conversely, however, this does not necessarily imply that a rather low retinal diastolic blood pressure value is accompanied with a decrease in pressure of the cerebrospinal fluid, nor, if the latter is normal, can it be inferred that the former is normal or low.

TABLE 8.—*Analysis of Values Obtained by Suganuma*[53e] *for Patients with Primary Contracted Kidney*

Age in Years, Inclusive	Number of Patients	Mean: Diastolic Blood Pressures, Mm.		Mean: Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Brachial	Retinal	
41-60 (1 patient of 61)	3 (3 eyes)	111	81	73

D'Osvaldo[53d] stated the opinion that the systemic vascular hypertension which later appeared in 3 of 10 patients with solitary cephalic hypertension, whom he previously had examined, already was present clinically, and probably

64. Berens, C.; Smith, H. T., and Cornwall, L. H.: Changes in the Fundus and in the Blood Pressure in the Retinal Arteries in Increased Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1151-1171 (Dec.) 1928.

65. Salvati, G.: La tension oculaire en position assise et couchée, Ann. d'ocul. **159**:128-130, 1922.

66. de Sanctis, R.: Il comportamento della P.A.R. (Pressione arteriosa retinica) nelle diverse posizioni del corpo, Internat. Cong. Ophth. (1937) **2**:119-137, 1938.

67. Klar, J.: Hypertonia arterialis retinae post commotionem cerebri, Internat. Cong. Ophth. (1937) **2**:52-56, 1938.

68. de Morsier, G.; Monnier, M., and Streiff, E. B.: La tension artérielle rétinienne dans les tumeurs intracraniennes, Rev. neurol. **71**:702-714 (June) 1939.

69. Pickering, G. W.: The Cerebrospinal Fluid Pressure in Arterial Hypertension, Clin. Sc. **1**:397-413 (Dec. 27) 1934.

should have been diagnosed as such, at the time of the first examination. Espildora-Luque [25c] and others found an elevation of retinal arterial pressures in patients with glaucoma, retrobulbar neuritis, intracranial tumors, meningitis, meningoencephalitis, cerebral trauma, myopia, optic neuritis, hereditary syphilis and the various forms of hypertensive disease and nephritic disease, all either with or without edema of the optic papilla. He classified this solitary cephalic hypertension into four types: cephalic, vertiginous, visual and neurologic, all depending, again, on whether the lesions appear to be intraocular or intracranial.

TABLE 9.—*Analysis of Values Obtained by Suganuma [53c] for Patients with Chronic Nephritis and with Secondary Contracted Kidney*

Age in Years, Inclusive	Number of Patients	Mean Diastolic Blood Pressures, Mm.		Mean Ratio of Retinal to Brachial Blood Pressure, Per Cent
		Brachial	Retinal	
16-40	14 (14 eyes)	116	81	70
41-60 (3 patients 61 to 76)	13 (13 eyes)	101	65	64
Mean: All patients.....		109	74	68

One wonders if a new category is necessitated by the group of 10 patients with allergy recently reported on by Gutmann [52] as having increased pressure in the central artery of the retina. This author was stimulated by his clinical findings to sensitize 5 rabbits with horse serum after initial ophthalmodynamometric readings were taken with his modified Bailliart instrument. He concluded that the later rise in intraocular vascular pressures in the animals was proof of successful sensitization and that the rabbits had become allergic; accordingly, he stated the belief that the higher pressures in the central arteries of his 10 patients were caused by the allergic status of their nasal mucous membranes.

Retinal arterial hypotension and its relation to the systemic arterial pressure and the intraocular tension have been studied in detail by both Lauber [70] and Sobánski.[71] Each stated the belief that there exists a minimum level of retinal diastolic blood pressure below which the capillary circulation functions only poorly. They expressed the opinion that systemic hypotension, particularly diastolic, accompanies progressive tabetic atrophy and that there is a subsequent lowering in the retinal diastolic arterial pressure from the normal range of 40 to 56 mm. of mercury, as determined by them. These authors stated that the optic nerve atrophy thus produced is subsequent to local ocular circulatory failure, since it was their belief that the local arterial pressure in this condition tends to decrease toward and below the level of the intraocular tension. Constantine,[44] who reviewed this field in her study of the interrelationship of retinal and systemic pressure in normal persons and in syphilitic patients, not only was unable to confirm either their work or their theories but found that the differential between the retinal diastolic arterial pressure and the intraocular pressure was higher than normal in patients with syphilis of the central nervous system, either with or without optic nerve atrophy. The brachial blood pressures she obtained generally were slightly higher in the latter group than in the normal patients.

Suganuma [53c] examined 36 eyes in 30 patients whose general examinations revealed the existence of asthma, hysteria, nervousness, beriberi, headache, arteriosclerosis and atherosclerosis, dizziness, nasal empyema, epilepsy, chronic nephritis, pregnancy, migraine, optic nerve atrophy, neuroretinitis, both of local and of systemic origin, acute choroiditis, peripheral neuritis and retrobulbar neuritis. It is not clear whether these clinical diagnoses were arrived at prior to or after the determination of the retinal pressures and their relationships to the other measurements obtained. These values have been analyzed by me in table 10 from the figures given by Suganuma. The significance of the mean values recorded in this table is not clear, although it will be observed that, while the percentage ratios closely approximate those obtained for the patients with systemic hypertension (tables 7, 8 and 9), the retinal diastolic pressures are almost midway in value between those ob-

TABLE 10.—*Analysis of Values Obtained by Suganuma [53c] for Patients with Solitary Cephalic Hypertension*

Age in Years, Inclusive	No. of Patients	Mean Blood Pressures, Mm.				Mean Ratio of Retinal to Brachial Blood Pressure, Per Cent	
		Systemic		Retinal			
		Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
8-15	1 (1 eye)	128	73	82	71	66	97
16-40	19 (22 eyes)	125	76	82	56	66	74
41-60 (1 patient of 72)	10 (13 eyes)	131	82	83	57	64	69
Mean: All patients.		127	78	83	56	65	71

70. Lauber, H.: Der Einfluss neidrigen allgemeinen Blutdruckes auf den Verlauf von Sehnervenerkrankungen, Wien. klin. Wchnschr. **48**:1079-1081 (Aug. 30) 1935.

71. Sobánski, J.: Das Wesen der tabischen Sehnervenatrophie und ihre Behandlung, Arch. f. Ophth. **135**:401-430, 1936.

tained by this author for patients with hypertensive disease and those obtained for normal persons, whereas the brachial diastolic pressures are in accord with the figures accepted as normal for the occidental races. The percentage ratios, however, of the retinal systolic to the brachial systolic pressures are consistently lower, although not notably so, than are those for the diastolic pressures. Suganuma did not comment on this particular point, but throughout all of his studies he appeared to stress the importance of the systolic rather than the diastolic retinal blood pressure. Parenthetically, the great majority of workers in both vascular manometry, or ophthalmodynamometry, and vascular micrometry seems to stress, for reasons not altogether clear, the systolic blood pressures and the arteriolovenous ratios respectively, rather than the associated diastolic pressures and the caliber of the arterioles and veins as distinguished from each other.

COMMENT

It is unfortunate that the few studies which have been carried out in some detail with reference to the various pressure relationships involved have not followed a relatively standard procedure with regard both to the ophthalmodynamometric methods and apparatus employed and to the classification of normal and of abnormal states according to uniform criteria of diagnosis. The reports in the available literature, however, with respect to investigations on the various vascular pressure relationships confront the worker in this field with an inescapable sense of the futility of efforts to arrive at any reasonably definite values for the normal retinal blood pressures. It becomes practically impossible therefore to rely diagnostically on the figures given by the various investigators for the retinal blood pressures in the numerous forms or stages of local and systemic hypertensive disease of whatever cause. It would appear to be much more reasonable to depend primarily on the information gained from a careful ophthalmologic examination, with particular reference to all of the changes that manifest themselves in the retinal vessels, particularly the arterioles, and in the retina and choroid as well, and these findings necessarily must be correlated with the results of the general physical examination.

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KERATITIS DUE TO N-BUTYL ALCOHOL

To the Editor:—In a recent report (An Unusual Type of Keratitis Associated with the Exposure to N-Butyl Alcohol [Butanol], ARCH. OPHTH. **33:** 106 [Feb.] 1945) describing keratitis in 28 workers exposed to n-butyl alcohol (butanol), we overlooked an article by M. Bücklers (Tröpfchenförmige Niederschläge auf der Hornhautoberfläche bei Möbelarbeitern, *Klin. Monatsbl. f. Augenh.* **99:** 676, 1937) describing what appears to have been the same condition in 7 furniture lacquerers. The causative agent was unknown to Bücklers, since the composition of the lacquer was an industrial secret; but the author's description of vacuoles ("not larger than 40 microns") situated symmetrically in the epithelium of otherwise clear corneas, the occurrence of severe epiphora, burning and watering of the eyes, and the complete reversibility of the process when the patients stayed away from their work leave little doubt that the keratitis which we described in connection with the use of n-butyl alcohol was, in fact, the same condition as Bücklers described in furniture workers. We assume, therefore, that the responsible agent in his cases was also n-butyl alcohol.

One of the outstanding differences between Bücklers' conclusions and ours, however, is in the matter of hypersensitivity. Since only a few of the employees in the industrial process with which Bücklers was concerned had complained of ocular irritation, the author assumed that some idiosyncrasy was necessary to account for the keratitis. In our series, on the other hand, we found that the majority of workers exposed to n-butyl alcohol vapor, including those who had no subjective symptoms, presented the characteristic corneal involvement and that the degree of involvement corresponded approximately to the concentration of the vapor. It did not seem necessary, therefore, to assume that the affected persons were hypersensitive.

NOTE.—We should like to take this opportunity of recording further pertinent data obtained since we submitted our first communication. We previously reported our failure to obtain corneal lesions in various animals exposed to n-butyl alcohol vapor. Since, however, butyl acetate was present along with butyl alcohol in connection with the cases reported by E. Krüger (Augenerkrankungen bei Verwendung von Nitrolacken in der Strohhutindustrie, *Arch. f. Gewerbepath. u. Gewerbehyg.* **3:** 798, 1932), we have exposed 6 guinea pigs and 6 albino rabbits to vapors of butyl acetate for varying lengths of time and examined their corneas periodically with the biomicroscope. As in the case of butyl alcohol, the results were negative. No abnormality was found in these animals after continuous exposure for ninety-six hours to 700 parts per million or to 1,100 parts per million nor for two weeks to 350 to 550 parts per million.

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News and Notes

EDITED BY DR. W. L. BENEDICT

PERSONAL NEWS

Leslie Dana Gold Medal Award.—The Leslie Dana Gold Medal, awarded annually for outstanding achievements in the prevention of blindness and the conservation of vision, will be presented this year to Dr. William Zentmayer, of Philadelphia, it is announced by the National Society for the Prevention of Blindness, Inc.

Dr. Zentmayer was selected for this honor by the St. Louis Society for the Blind, through which the medal is offered by Mr. Leslie Dana, of St. Louis. This highly prized token of recognition in the field of public health is given on the recommendation of the Association for Research in Ophthalmology.

Despite his eighty years, Dr. Zentmayer is in active practice as an ophthalmologist. He is professor emeritus of diseases of the eye, Graduate School of Medicine, University of Pennsylvania, and consulting surgeon to Wills Hospital, St. Mary's Hospital and Glen Mills School, all in Philadelphia. He received his degree of Doctor of Medicine from the University of Pennsylvania School of Medicine in 1886.

Dr. Zentmayer is a member of numerous medical, public health and other scientific organizations. He has served as president of the American Ophthalmological Society; chairman of the Section on Ophthalmology, American Medical Association; chairman of the section on ophthalmology, College of Physicians, Philadelphia; editor of the College of Physicians of Philadelphia Transactions and Studies; associate editor, ARCHIVES OF OPHTHALMOLOGY, and chairman of the section on eye, ear, nose and throat, Medical Society of the State of Pennsylvania. He is a member of the board of directors of the National Society for the Prevention of Blindness, Inc.

The conditions of the Leslie Dana Gold Medal award set forth that it is to be made for "long meritorious service in the conservation of vision in the prevention and cure of diseases dangerous to eyesight; research and instruction in ophthalmology and allied subjects; social service for the control of eye diseases; and special discoveries in the domain of general science or medicine of exceptional importance in conservation of vision."

GENERAL NEWS

Graduate Course in Ophthalmology and Otolaryngology, Gill Memorial Eye, Ear and Throat Hospital.—The nineteenth annual spring graduate course in ophthalmology and otolaryngology will be held at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Va., April 1 to 16, 1946.

Second Pan-American Congress of Ophthalmology.—The official meeting place of the Second Pan-American Congress of Ophthalmology, which will take place in Montevideo, Uruguay, Nov. 26 to Dec. 1, 1945, is the Municipal Hotel, Miramar, on Carrasco Beach. This is a first class, modern hotel, and the city of Montevideo has fixed the reduced rate of $5 per day for room and meals for congress guests. Inasmuch as all program sessions, the scientific and commercial exhibits and social affairs will take place in that hotel, it will be convenient for congress guests to stay there. Reservations may be made through Dr. Conrad Berens, 301 East Fourteenth Street, New York 3. Such requests should include the names of all persons in the party.

Any one who desires to stay in some other hotel should make requests for reservations to the treasurer of the congress, Dr. Julio A. Sicardi, Agrupación Universitaria, Ave. Agracida 1464, P. 13, Montevideo, Uruguay.

The registration fee for members of the congress is $11 United States money ($20 Uruguayan), and for others in the party who wish to be included in the social events, $5.50 United States money, per person. These fees may also be paid in advance to Dr. Berens.

Because of general travel conditions, it was not possible to make arrangements for persons attending the congress from the United States to go in a group. The Pan-American Airways and the American Express Company will cooperate in doing everything possible to work out transportation plans to meet individual requirements.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

CONCERNING THE RELATIONS OF THE DEVELOPING OPTIC NERVE TO THE RECESSUS OPTICUS AND THE HYPOPHYSIS IN YOUNG FOETUSES: A STUDY OF SEVEN HUMAN FOETUSES 4 MM. TO 40 MM., INCLUSIVE. H. C. HADEN, Am. J. Ophth. **27:** 1 (Oct., pt. 2) 1944.

The sixth de Schweinitz Lecture, delivered before the Section on Ophthalmology of the College of Physicians, Philadelphia, appears as a supplement to the October issue of the *American Journal of Ophthalmology*. It contains a number of illustrations but does not lend itself to abstracting.

W. S. REESE.

Conjunctiva

LOCAL PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM. SORSBY and E. HOFFA, Brit. M. J. **1:** 114 (Jan. 27) 1945.

The authors state that, unlike the sulfonamide compounds, penicillin remains effective in the presence of pus. It therefore has great possibilities for the local treatment of ophthalmia neonatorum in place of general sulfonamide treatment. Forty-seven infants in the ophthalmia neonatorum unit at White Oak (London County Council) Hospital were treated with penicillin. The concentrations began at 500 Oxford units per cubic centimeter and were gradually increased to 2,500 units; the doses were instilled at half hour intervals for the first three hours, then hourly for twenty-four hours and every two hours thereafter.

In a comparison of penicillin therapy and general sulfonamide treatment, the authors speak of the advantages of local treatment and avoidance of the danger of sensitization. At the same time, frequent irrigations are a trial to the infant and a considerable burden to the nurse. As the concentrations were increased from 500 to 2,500 units, there was an increasing proportion of satisfactory results. The authors conclude that in adequate concentration penicillin appears to be effective against all the common causal organisms of ophthalmia neonatorum, including the virus of inclusion blennorrhea. It is likely that some forms of ophthalmia neonatorum respond more readily to penicillin than others, but on the whole the results are of the same order as those obtained with the sulfonamide compounds.

ARNOLD KNAPP.

Congenital Anomalies

UNUSUAL PRELACRIMAL CONGENITAL MALFORMATION. M. SORIA ESCUDERO, Arch. Soc. de oftal. hispano-am. **3:** 471 (Nov.-Dec.) 1943.

A boy 6 years of age presented a small congenital sinus, about 2 mm. deep, in the region of the lacrimal sac, immediately below the canthal ligament. There was no connection with the sac.

The author has been unable to find in the literature any previous report of such a condition.

H. F. CARRASQUILLO.

A CASE OF PERSISTENCE OF THE HYALOID ARTERY: INTERESTING ASPECT OF ITS OPHTHALMOSCOPIC IDENTIFICATION. N. P. DE FIGUEIREDO, Rev. brasil. de oftal. **2:** 121 (March) 1944.

De Figueiredo identified the hyaloid artery in the eye of a man 26 years of age. The patient exhibited dental abnormalities of intrauterine origin. The author believes that the persistence of the hyaloid artery depends on a sudden cessation of the involution of the artery during the last few months of intrauterine life due to syphilis, which increases in virulence during the last few months of pregnancy. Syphilis is also the cause of the dental abnormalities which are often associated with persistence of the hyaloid artery.

W. ZENTMAYER.

General Diseases

OPHTHALMOLOGIC LESIONS ENCOUNTERED IN TROPICS, WITH SPECIAL REFERENCE TO OCULAR MANIFESTATIONS OF MALARIA. J. N. ROBERTSON, North Carolina M. J. **5:** 483 (Oct.) 1944.

According to Robertson, optic neuritis and amblyopia are at times associated with malaria. This form of amblyopia has to be differentiated from that which is due to quinine. In the latter the condition depends on the retinal anemia resulting from the toxic spasm of the arterioles: there are extreme pallor of the optic disks and contraction of the visual fields. This picture is in contrast to the hyperemic disk and retina associated with malarial toxemia. Malarial amblyopia occurs as a result of the action of the malarial toxin on the optic nerve and retina. Often optic neuritis and papillary edema result from the blocking of the retinal and choroidal vessels by parasites and leukocytes. The retinal

hemorrhages are usually small, multiple and peripheral; large macular hemorrhages do occur with the malignant types of malaria. Ulceration of the cornea is the most common ocular sequela of malaria, and recurrent iritis is frequently associated with this keratitis. Supraorbital neuralgia precedes the corneal lesions. Photophobia and lacrimation are characteristic signs and often precede the corneal lesions by days or weeks. On an island in the Southwest Pacific the author encountered many patients with intraocular disturbances among men between the ages of 20 and 30. Many had suffered some depletion of the powers of accommodation and convergence, as was manifested by the complaints of difficulties in reading, scotomas and muscular imbalance, particularly exophorias. Subjectively, the complaints were loss of vision, frequent headaches in the occipital or temporal region, dizziness, pain in the eyeballs, tenderness on palpation, photophobia, lacrimation and spots before the eyes. The objective findings were irregularity of the pupils; retinitis of the atrophic type, usually in or around the macular area; unusual concentration of choroidal pigmentation; generalized hyperemia of the retina and nerve head; optic neuritis, both mild and severe, optic nerve atrophy, and, in a few cases, severe progressive choroidoretinitis and uveitis. Some of the patients who were evacuated were followed up by the author after his return. Some of these men now have chronic uveitis.

J.A.M.A. W. ZENTMAYER.

General Pathology

HISTOLOGIC NOTES: (A) PRESENCE OF ANOMALOUS FORMS OF CONES IN NORMAL RETINAS. (B) DEGENERATIVE LESION IN THE CONES IN A CASE OF OVERDOSE IN THE THERAPEUTIC USE OF ROENTGEN RAYS. A. GALLEO FERNANDEZ, Arch. Soc. oftal. hispano-am. **4:** 177 (March-April) 1944.

Galleo Fernandez made his observations on the previously normal eye of a man 38 years of age which was enucleated on account of a severe penetrating wound and on an eye which was removed after the incorrect use of roentgen rays in treatment of a carcinoma of the upper lid. In the first eye, using the technic of Balbuena, the author observed that in the region of the macula some cones had their nuclei located immediately above the external limiting membrane, and not below it, as generally occurs. In the other eye, besides all the generalized histologic changes in the ocular tissues, he noted lesions in the retina which up to the present have not been fully studied. Crowding of Nissl granules in the ganglion cells was observed. The nuclear layers showed no change except infiltration with blood cells. The author calls attention to the changes seen in some of the cones. There were thickening and retraction of the internal filament, and large vacuoles appeared in the foot plates. These changes occurred only in the cones in the region of the macula.

H. F. CARRASQUILLO.

Glaucoma

VOGT'S CYCLODIATHERMY PUNCTURES IN TREATMENT OF GLAUCOMA. A. PALOMAR PALOMAR, Arch. Soc. oftal. hispano-am. **4:** 608 (July-Aug.) 1944.

The author discusses in detail this method of treatment for glaucoma. He states that in spite of the gratifying results shown in statistics published up to this time and of his own work it is erroneous to believe that this new method may supplant other operations which are now in continual use. He gives the following indications for this new procedure: (1) hemorrhagic glaucoma; (2) acute glaucoma when medical treatment or basal iridectomy has failed; (3) glaucoma secondary to iridocyclitis when iridectomy has not been successful; (4) painful absolute glaucoma when other procedures have failed; (5) glaucoma associated with aphakia or luxation of the crystalline lens; (6) secondary glaucoma with adherent leukoma, when iridectomy has failed; (7) all forms of glaucoma when the anterior chamber has disappeared, as a primary operation or after some other procedure has failed; (8) chronic simple glaucoma when the visual fields have been much reduced; (9) all forms of glaucoma when other operations have failed or any other intervention is likely to produce total loss of vision.

H. F. CARRASQUILLO.

HEMICYCLODIALYSIS AND ITS USE IN TREATMENT OF CHRONIC SIMPLE GLAUCOMA. E. GRAUE JR., Bol. d. hosp. oftal. de Nuestra Señora de la Luz **2:** 51 (Sept.-Dec.) 1942.

Graue uses what he calls hemicyclodialysis as the operation of choice for simple glaucoma. The operation is a modification of the cyclodialysis procedure of Heine, which, without knowledge of the author, was advocated by Elschnig some years before. It consists in performing a disinsertion of the ciliary muscle in half of the circumference of the limbus according to the technic of Heine. The results after this operation, according to the author, are better than those in any other type of surgical procedure.

H. F. CARRASQUILLO.

Lacrimal Apparatus

PSEUDODACRYOCYSTOBLENNORRHEA. M. LOPEZ ENRIQUEZ, Arch. Soc. de oftal. hispano-am. **3:** 474 (Nov.-Dec.) 1943.

The author gives this name to a process characterized by anatomicophysiologic integrity of

the lacrimal sac accompanied with persistent lacrimation and a continuous purulent secretion through one of the lacrimal puncta.

Two cases are reported. The condition was produced by a fistulous tract, established from a previous chalazion, which opened into the lacrimal sac.

H. F. CARRASQUILLO.

ABORTIVE TREATMENT OF DACRYOCYSTITIS. L. ORTIN, Arch. Soc. de oftal. hispano-am. **3**:476 (Nov.-Dec.) 1943.

Dacryocystitis may occur as an inflammation of the tear sac itself or as a pericystic process with or without involvement of the sac. The pericystic condition may arise from a previously diseased sac or may be a blood-borne infection with no relation to any pathologic condition of the sac. The canaliculi and the lacrimal duct may or may not be occluded.

Conservative initial treatment may avoid surgical intervention. If the canaliculi are impervious and there is suppuration within the sac, the lumen is opened by injecting under pressure a few drops of a solution containing 5 or 10 per cent cocaine in a 1 : 1,000 solution of epinephrine hydrochloride. The sac is emptied by pressure and then irrigated with a 3 per cent solution of boric acid, followed by a lotion containing mercury oxicyanide (1 : 4,000). The same procedure is repeated next day, and then a few drops of 1 or 2 per cent silver nitrate is injected into the sac, followed by irrigation with water if there is retention. If complete obstruction of the canaliculi exists, a no. 1 probe may be used to dilate the opening. If there is inflammation around the sac secondary to infection of the sac, the same treatment is given. However, if pus forms, an incision should be made, but this should not go deep into the cavity of the sac.

H. F. CARRASQUILLO.

Lids

ALOPECIA AREATA (PELADA) OF THE EYELIDS. H. MARBACK, Arq. brasil. de oftal. **6**: 211 (Dec.) 1943.

Marback reports the case of an adolescent boy of 14 years who presented total alopecia areata (pelada) of the left upper eyelid. The eyes showed no other abnormality and functioned normally. The age of the patient at the time the condition appeared was not known. There was no history of local trauma or of the use of any local drug. One of the parents had syphilis. The patient was observed for about two months, during which the alopecia was limited to the left upper eyelid. Antisyphilitic therapy, consisting of administration of quinine bismuthiodide, was carried out for about three months, in the course of which the eyelashes reappeared and grew normally; they became permanent and were still present at the time of the report, two years and a half after discontinuation of the therapy.

W. ZENTMAYER.

MARCUS GUNN'S PHENOMENON. J. DE PAULA XAVIER, Arq. brasil. de oftal. **6**: 213 (Dec.) 1943.

De Paula Xavier reports the case of a boy 11 years of age who presented the jaw-winking phenomenon on the right side. The syndrome had been present from infancy. The patient was otherwise normal. There was right hypertropia and amblyopia ex anopsia of the right eye. Blepharoptosis was pronounced. The involved eye opened when the patient opened the mouth or made masticatory movements to either side with the mouth either closed or opened, when the chin was projected and when the frontalis muscle was contracted. The Wassermann reaction of the blood was negative. The mother had had two abortions.

Surgical intervention may lessen the blepharoptosis. In some cases the blepharoptosis is decreased by compensatory contraction of the frontalis muscle. Progressive improvement in spontaneous opening of the eye can be expected as the child grows to adult life. Operation is indicated early in adult life if there is still conspicuous blepharoptosis. The patient was instructed in using the frontalis muscle for opening the eye.

W. ZENTMAYER.

Neurology

LOCALIZATION OF CEREBRAL LESION. P. FALCAO, Arq. brasil. de oftal. **7**: 1 (Feb.) 1944.

Falcao directs attention to the value of ocular neurologic symptoms in the diagnosis of the site of a cerebral lesion. A destructive lesion of the optic nerve causes total blindness of the eye. A medial sagittal lesion of the optic chiasm with involvement of the nasal crossed optic fibers causes bitemporal heteronymous hemianopsia, which may be peripheral, central or total, according to whether the site of the lesion is in the anterior, the posterior or the anteroposterior aspect of the optic chiasm. A lesion in the left or the right segment of the posterior pole of the optic chiasm or in the corresponding part of the optic tract causes right or left homonymous hemianopsia. If the lesion is located at a point on the optic tract before it reaches the anterior corpora quadrigemina, hemianopsia and motor disorders of the sphincter of the iris occur. If the lesion is located in the visual center of the calcarine fissure, or near this center, quadrantic homonymous hemianopsia, either superior or inferior, according to the site of the lesion, is produced. A lesion in an area of the cortex which is in communication with the cortical visual zone causes cortical or psychic blindness or else alexia. The Argyll Robertson pupil is a sign

of neurosyphilis. Adie's anisocoria is a neurotropic disorder. It is also a component of the Adie syndrome (encephalomeningopathy). Oculomotor paralysis on one side and hemiplegia on the opposite side (Weber's syndrome) indicates a lesion of the oculomotor nerve before it emerges from the lower border of the cerebral peduncle. Unilateral miosis, ptosis and enophthalmos (Horner's syndrome) result from paralysis of the cervical sympathetic fibers. Purely motor total ocular paralysis, of the Rochon-Duvigneau type, indicates a lesion of the oculomotor nerve in its course through the sphenoid fissure. Sensorimotor paralysis occurs when the ophthalmic nerve is also involved. Total motor-sensory paralysis occurs when the traumatic lesion or the tumor involves the optic tract. The sixth nerve is paralyzed in the Gradenigo syndrome, as a result of a lesion of the petrous bone, and also in association with other nerves in diseases of the pons which produce the Millar-Gubler syndrome (alternating abducens-facial hemiplegia). Corneal anesthesia (Oppenheim's sign) is an early sign of tumor of the cerebellopontile angle. The oculocardiac reflex shows the relations between the trigeminal and the spinal nerves. The various modalities of nystagmus during stimulation of the vestibular nerve are of value in the differential diagnosis of cerebellar and labyrinthine lesions, as well as in the diagnosis of the site of certain cerebral tumors.

W. ZENTMAYER.

POST-TRAUMATIC AND HISTAMINE HEADACHE. A. FRIEDMAN and C. BRENNER, Arch. Neurol. & Psychiat. **52:** 126 (Aug.) 1944.

Twenty-two patients with a history of headache following injury to the head received 0.1 mg. of histamine base (0.275 mg. of histamine diphosphate) intravenously.

Headaches were produced by this injection which in 13 patients were identical with the post-traumatic headaches in character and location and in 3 patients were strikingly similar. In 2 patients headache failed to develop.

The prompt decrease in systolic blood pressure after the injection of histamine was followed by a secondary rise which was nearly as great (22 and 18 mm. of mercury, respectively). This rise was probably due to a response of the sympathetic nervous system produced reflexly by the primary changes incident to the injection of histamine.

Headache appeared as the blood pressure was rising.

The majority of the patients with histamine headache obtained some (occasionally striking) relief by sitting upright. This is inconsistent with reports in the literature that lowering of the intracranial pressure of the cerebrospinal fluid aggravates histamine headache.

It is possible that the injection of histamine activates the physiologic mechanism which is involved in the production of some types of post-traumatic headache.

The possibility that the injection of histamine may influence favorably the symptom of post-traumatic headache is suggested by results in some of our patients.

R. IRVINE.

Orbit, Eyeball and Accessory Sinuses

UNILATERAL PULSATING EXOPHTHALMOS CAUSED BY RUPTURE OF THE CAROTID ARTERY IN THE CAVERNOUS SINUS OF THE OPPOSITE SIDE: REPORT OF A CASE. F. GEIS, Klin. Monatsbl. f. Augenh. **106:** 209 (Oct.) 1941.

A youth aged 18 fired a 6 mm. caliber bullet into his right temple. He was able to return to work after about ten weeks, free from any disturbances except for a bruit, which increased while he was working or stooping. A week after he had resumed his work, or eleven weeks after the accident, he noticed that his left eye protruded. The bullet had passed through the right temporal bone behind the orbit and rested on the right side of the dorsum sellae at the right cavernous sinus. The presence of several bone splinters was noted in the roentgenogram. The oculomotor, trochlear and optic nerves were injured, while the abducens and maxillary nerves, located in the lower portion of the sinus, were intact. Rupture of the right internal carotid artery in the right cavernous sinus occurred and was followed by dilatation of the venous system, which caused pulsating exophthalmos on the opposite side, while the orbit on the side of the ruptured carotid artery remained unaltered. This type of crossed pulsating exophthalmos may occur if the blood stream returning from the cavernous sinus in the ophthalmic vein of the same side is blocked by tear, thrombosis or compression of the superior ophthalmic vein through splinters of bone or a foreign body. Previous enlargement of the intercavernous sinuses may further the development of crossed pulsating exophthalmos. The bruit ceased on compression of the carotid artery on the right (opposite) side and, later, after its ligation. It is advisable prior to ligation to find out by compression which carotid artery is the cause of a pulsating exophthalmos.

K. L. STOLL.

Retina and Optic Nerve

EXUDATIVE RETINITIS (COAT'S DISEASE): C. S. DAMEL and A. D. GRAMMATICO, Arch. de oftal. de Buenos Aires **19:** 51 (Feb.) 1944.

A girl 18 years of age had involvement of both eyes. She was suffering from syphilis, probably hereditary. The general examination revealed nothing else of importance. The authors

had the opportunity to observe the patient for seven months and noticed that the exudate in the left eye, which was the last involved, changed from gray to white; this, according to them, furnished proof of the hypothesis that the condition has its origin in a degenerative process of the pigmentary epithelium.

A full discussion of the etiopathology and differential diagnosis is given.

H. F. CARRASQUILLO.

TOXICITY OF ARSENICAL COMPOUNDS FOR THE OPTIC NERVE: CONTRAINDICATIONS. D. LIVRAMENTO PRADO, Arq. brasil. de oftal. **7**:61 (April) 1944.

According to Prado, the majority of persons with neurosyphilis have lesions of the optic nerve, latent, active or healed. Syphilis gives to the nerve a special sensitivity to arsenicals, which is the cause of the development of optic neuritis in the course of arsenical therapy when the latter is given without primary treatment with bismuth or mercury. The author advises a thorough ophthalmologic examination of the patients before administration of antisyphilitic treatment. Any lesion of the fundus of the eye, even if healed, as well as keratitis or progressive diminution of the visual field, contraindicates immediate administration of arsenicals. These patients should have bismuth or mercury therapy until the ocular lesion shows great improvement. After a period of rest from the use of bismuth or mercury, arsenical therapy may be administered without danger of the development of optic neuritis.

W. ZENTMAYER.

Therapeutics

OCULAR THERAPY WITH PENICILLIN USED TOPICALLY, INTRAOCULARLY, AND SYSTEMICALLY. C. A. MIETUS, Am. J. Ophth. **28**: 173 (Feb.) 1945.

Mietus gives the following summary:

"1. Penicillin is a wonderful new therapeutic agent which can safely be added to the armamentarium of ophthalmologists.

"2. Penicillin can be utilized in the three ways demonstrated in the foregoing case reports.

"3. The use of penicillin by injection into the anterior chamber offers promise of beneficial results, and this mode of therapy warrants further investigation."

W. S. REESE.

PENICILLIN IN OPHTHALMOLOGY. J. E. L. KEYES, J. A. M. A. **126**:610 (Nov. 4) 1944.

Material for this report was derived from the special penicillin research center at Bushnell General Hospital, from private communications from medical officers of the Army and from medical literature on penicillin.

Penicillin is the drug of choice in the treatment of ophthalmic diseases secondary to infection with gonococci, streptococci and sensitive staphylococci. Penicillin should be given a trial in the treatment of diseases caused by Neisseria meningitidis, Neisseria catarrhalis and the pneumococcus. The use of penicillin is optional in the treatment of infections caused by Corynebacterium diphtheriae, Clostridium welchi, Actinomyces bovis and Treponema pallidum. In diseases due to noninfectious processes, such as allergy, the removal of a secondary infection by treatment with penicillin is helpful but obviously leaves the primary problem unsolved. The use of penicillin as a prophylactic with certain intraocular operations and ocular injuries is recommended. Early and large doses of penicillin are indicated in cases of orbital cellulitis secondary to infection in the paranasal sinuses and the adjacent dural sinuses.

Solutions of penicillin, because of their instability, do not lend themselves to office and home medication as readily as do more stable drugs. Penicillin ointment is reasonably stable for at least a month at room temperature and for six months in a commercial refrigerator. Routes of administration and dosages are stated.

The article, which is comprehensive, is illustrated.

W. ZENTMAYER.

Society Transactions

EDITED BY DR. W. L. BENEDICT

AMERICAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

CONRAD BERENS, M.D., *Chairman*

ROBERT J. MASTERS, M.D., *Secretary*

Ninety-Fourth Annual Session, Chicago
June 12 to 16, 1944

The Making of an Opthalmologist. Chairman's Address. DR. CONRAD BERENS, New York.

The medical curriculum of the ophthalmologist should include comprehensive courses in higher mathematics, biology, chemistry, physics and modern languages and, if possible, elementary courses in embryology, comparative anatomy, physiology, bacteriology and physiologic chemistry. In medical school the student should be permitted to elect certain subjects which will aid him in ophthalmology. After graduation from the medical school, a year of internship and two or more years of residency in an eye hospital or the ophthalmic department of a general hospital are most desirable. If possible, the student should have a course in the basic sciences related to ophthalmology before he enters active hospital work. One of the most important problems in ethics from the standpoint of public service and public health is that of optometry. The lack of cooperation between ophthalmologists and all others concerned with vision and health of the eyes is the most serious unsolved problem in the prevention of blindness today.

Participation in the scientific program at medical meetings is urged, so that the ophthalmologist will maintain his interest in general medicine, surgery and neurology.

Diagnosis of Orbital Tumors. Address of the Guest of Honor. DR. WILLIAM L. BENEDICT, Rochester, Minn.

The three cardinal signs of orbital tumor are, in order of their importance, exophthalmos, visual disturbances and changes in bone as revealed in roentgenograms. Exophthalmos is the most common of all these signs of tumor of the orbit. As it occurs also in all cases of space-taking or expansive disorders within the orbit, anterior or ocular displacement in itself is not indicative of the cause. Generally speaking, the rate of increase in proptosis is an index of the rate of growth or expansion of the space-taking lesion behind the eyeball; but when proptosis is caused by a tumor, its extent is not truly indicative of the size of the lesion, as tumors of the anterior part of the orbit, particularly in the superior quadrant, will as a rule produce exophthalmos in the early stages of their development, and, since the globe occupies most of the space in the anterior third of the orbit, any extraocular growth displaces the eyeball as long as the bony wall stands firm. Tumor of the posterior half of the orbit, on the other hand, may acquire considerable size before appreciable proptosis occurs.

As most tumors of the orbit are unilateral, unilateral exophthalmos may be presumed to be due to a tumor unless there is some other evidence of cause for it. Bilateral exophthalmos due to tumors of the orbit is rare but is commonly present with Mikulicz' disease (achroacytosis of lacrimal gland) and with dysthyroidism. Angioneurotic edema and lymphoblastoma are also most frequently bilateral and may resemble neoplasms. Mucocele, pyocele or aneurysm causing exophthalmos is often undiagnosed or is mistaken for a tumor. To rule out goiter as a cause of exophthalmos may require observation of the patient under treatment for several months. Mikulicz's disease may closely resemble the orbital changes of hyperthyroidism.

Loss of visual acuity, with preservation of vision in the peripheral field, strongly indicates a postorbital or chiasmal lesion. When central loss of vision occurs before exophthalmos appears, the chances are greatly in favor of the lesion being due to an inflammatory process and of loss of vision being produced by such condition as retrobulbar neuritis.

In the absence of ophthalmoscopic changes, such as choked disk, optic neuritis, optic nerve atrophy, retinal and choroidal disease and opacities of the media, visual loss may be presumed to be due to changes along the visual pathways. The lesion may be retrobulbar and may be situated within the orbit. There is always the probability that it may be due to a tumor. Roentgenograms are useful in the identification of some orbital tumors. Osteomas of the sinuses that encroach on the orbit are best identified by this means. Hyperostosis of the orbital wall is brought about by tumors and diseases of the bone or of soft tissue that is situated near the bone.

Some vascular tumors that develop slowly along the orbital wall produce hyperostosis. Erosion of the walls is the rule in cases of pulsating tumor, although thickening of the lateral wall of the orbit may occur, as in cases of

hemangioma and pulsating exophthalmos. Exploration of the orbit for diagnosis should always be made through an incision large enough and so placed that, should a tumor be encountered or any other pathologic condition be found that would require surgical removal, the operation can be completed at the time. If one is not sure of the presence of a tumor, it is safe in most instances to apply roentgen therapy and await developments.

Treatment of Bilateral Retinoblastoma (Retinal Glioma) Surgically and by Irradiation: Report on Progress. Dr. Hayes Martin and Dr. Algernon B. Reese, New York.

This article was published in full in the June 1945 issue of the Archives, page 429.

Keratitis Neuroparalytica: Corneal Lesions Following Operations for Trigeminal Neuralgia. Dr. C. L. Pannabecker, Ann Arbor, Mich.

This article was published in full in the December 1944 issue of the Archives, page 456.

ABSTRACT OF DISCUSSION

Dr. A. D. Ruedemann, Cleveland: In the treatment of trigeminal neuralgia the surgeon should not cut the first division of the nerve. After operation for trigeminal neuralgia the patient should be under the observation of a physician at home. His general health must be maintained.

Major J. M. Masters, Medical Corps, Army of the United States: Impressions gained from the study of about 15 patients who were treated either by total or by subtotal posterior ganglionectomy or rhizotomy in the neurosurgical service of Dr. E. Vernon Hahn, of Indianapolis, were subsequently confirmed by the study of other patients similarly treated. Loss of luster of the corneal epithelium soon after operation, with the appearance of a faint gray path, was nearly always observed, causing apprehension of a catastrophe which did not always occur. From one to three days after operation a fine stippling of the involved cornea may be observed after staining with fluorescein. This stippling is seen much earlier than the more serious corneal complications mentioned by Dr. Pannabecker. Their presence indicates cellular edema and fine exfoliation of the epithelium. Usually they leave five to seven days after operation without secondary scarring, but they have been observed to last many weeks without going on to ulceration. Frequent relapses may occur during the process of healing.

The observation has never been made in cases of subtotal rhizotomy in which the ophthalmic division of the nerve has been spared.

Meridional Aniseikonia at Oblique Axes. Dr. Herman M. Burian and Dr. Kenneth N. Ogle, Hanover, N. H.

This article was published in full in the April issue of the Archives, page 293.

ABSTRACT OF DISCUSSION

Dr. Lawrence T. Post, St. Louis: My studies on aniseikonia made personally on more than 450 patients, as well as less personal observations on about 700 patients during the past ten years, have been concerned with practice rather than theory. The figures which my associates and I have obtained indicate that about 80 per cent of patients for whom aniseikonic glasses were ordered were definitely helped and that almost 50 per cent were made entirely comfortable. Replies were solicited only from persons who had worn their aniseikonic correction for at least nine months.

The first question which arises is whether the major factor in this increased comfort is the correction of aniseikonia or something else, such as a change in the refractive correction made at the time the eikonic lenses were given or the psychologic effect of the elaborate examination. It may also be asked whether the patient could have been relieved by some procedure other than the giving of the eikonic glasses, for example, orthoptic training. I have the impression that the eikonic correction is by far the most important factor in producing this increased comfort.

Aniseikonia can never be fully evaluated clinically or the eyes attain their maximum usefulness until two conditions have been fulfilled: First, the test must be made available to every ophthalmologist, and, second, the cost of eikonic lenses must not be prohibitive to the average patient.

Dr. Ernest A. W. Sheppard, Washington, D. C.: Early students of modern refraction and of ocular motility recognized deviations of the vertical meridians of the eyes. Stevens designated such a deviation as the declination error, and he and Savage emphasized its importance as a cause of asthenopia. The types of declination errors were not clearly understood, and therefore the treatment was unsatisfactory. Burian and Ogle have described three types, on the basis of the etiologic factors: (1) declination errors produced by cylindric lenses at oblique axes; (2) deviation errors associated with cyclophoria, and (3) deviation errors associated with basic meridional aniseikonia.

For diagnostic purposes it is more important to know the type than the degree. The methods of measurement used by the authors constitute an important advance both in refraction and in ocular motility, and they are to be congratulated on having recognized the association of the two conditions. The results they have obtained are most gratifying.

Gonioscopic Correlates of Responsiveness to Miotics. Dr. Peter C. Kronfeld, Chicago.

This article was published in full in the December 1944 issue of the Archives, page 447.

ABSTRACT OF DISCUSSION

Dr. H. Isabelle McGarry, Chicago: In cases of glaucoma of the narrow angle type, Dr. Kronfeld mentions the frequent presence of pronounced angle predicament without peripheral anterior synechias. In many cases in which the angles in the two eyes appear exactly the same, one eye may show a notable increase in tension, requiring miotics or surgical treatment or both, and the other eye may not show hypertension unless provoked by mydriasis. In the clinic, my associates and I consider the eye with the normal pressure, normal fields and normal disks as preglaucomatous, and prevent mydriasis with miotics.

I, also, have been unable to come to any definite conclusion regarding glaucoma of the wide angle type and glaucoma secondary to iridocyclitis.

Dr. John M. McLean, New York: Gonioscopy, while of restricted usefulness to the pure clinician, is a valuable tool in the hands of the clinical investigator. It has already demonstrated the fallacies of the theories which explain chronic simple glaucoma on the basis of anterior peripheral synechias. It has also shown that synechias are the result, not the cause, of chronic congestive glaucoma.

Dr. Kronfeld had demonstrated a correlation between miosis itself and reduction of tension in certain cases of glaucoma of the iris block type. This does not hold true in all cases of this type, nor does it hold for other forms of glaucoma. Moreover, all who practice routine gonioscopy in the study of glaucomatous eyes find many cases in which there are open angles and an elevated intraocular pressure which responds to use of the miotic drugs.

Dr. C. W. Ascher, Cincinnati: If gonioscopic examination does not supply correlates of responsiveness to miotics, a test of the efficiency of the exhaust system can be performed in cases in which, under favorable conditions, the outflowing aqueous humor may become biomicroscopically visible. This occurs in a vein arising from the corneal limbus or, still farther away, in a vein leaving a scleral emissarium. These vessels which contain aqueous humor, either clear or mixed with blood, have been called aqueous veins.

Compression of the recipient vessel of an aqueous vein produces either expulsion of blood from the blocked section of the vessel or expulsion of clear fluid from the particular aqueous vein. In glaucomatous eyes the latter effect is the rule, indicating weak elimination of aqueous humor from this aqueous vein, and possibly from the whole exhaust system, probably due to a transient or, in other cases, to a permanent narrowing of the immediate outlets of the canal.

Miotics, as well as surgical intervention, can reestablish a more vigorous flow in favorable cases, and then expulsion of blood from the blocked section of the vessel may be seen during the compression test performed on the aqueous vein.

Choice of Operation in Glaucoma. Dr. Paul A. Chandler, Boston.

Operation is nearly always indicated in cases of primary acute glaucoma. Iridectomy will not be successful in cases in which the condition has been neglected. In these cases a filtering operation of some sort must be done if tension is to be permanently controlled. Probably an iridencleisis with sclerectomy is the most effective operation. In cases of chronic glaucoma the choice of operation depends mainly on the personal preference of the surgeon. There are some situations, however, which seem to respond better to certain types of operation. Trephination is very effective in younger persons, particularly when the tension of the glaucomatous eye is relatively low. After the age of 60 iridencleisis is probably preferable, since it seldom produces hypotony and offers little trauma to the eye. With congested eyes iridencleisis with sclerotomy is very satisfactory. In general, the iris inclusion operation is chosen whenever an eye must be operated on in the presence of a relatively high tension.

Dibutoline Sulfate: A New Mydriatic and Cycloplegic Drug. Dr. Kenneth C. Swan and Dr. Norman G. White, Iowa City.

This article was published in full in the January issue of the Archives, page 16.

Management of Traumatic Hyphemia. Dr. Ralph O. Rychener, Memphis, Tenn.

Traumatic hyphemia following contusion rather than laceration of the globe is frequently complicated by secondary hemorrhage from the iris, increased intraocular pressure, staining of the cornea with blood, atrophy of the iris and persistent secondary glaucoma, which may result in atrophy of the optic nerve and staphyloma of the cornea. Most of these complications may be avoided or the effect nullified by simple paracentesis of the cornea as soon as the intraocular pressure is elevated; the procedure is also indicated when the anterior chamber is completely filled with blood, even though the pressure may still be normal. Surgical intervention should be carried out without delay whenever the intraocular pressure is increased or no clear aqueous is visible in the anterior chamber. It is possible that the use of miotics rather than mydriatics

immediately after injury will result in fewer secondary hemorrhages and in less necessity for surgical measures.

ABSTRACT OF DISCUSSION

Dr. F. Bruce Fralick, Ann Arbor, Mich.: Partial filling of the anterior chamber is not an indication for paracentsis. These hemorrhages usually absorb in a few days and seldom cause any elevation in tension. Complete filling of the anterior chamber with blood is definitely an indication for paracentesis, whether the tension is elevated or not. One should not wait for elevation of tension before doing the paracentesis.

By judicious use of this procedure, the course of the absorption period has been shortened and the incidence of hemorrhagic staining of the cornea has been lowered. My associates and I employ atropine in eyes displaying traumatic hyphemia with the thought of combating the associated iridocyclitis. Dr. Rychener has suggested that miotics be used in place of atropine at this stage. There are no comparable statistics to support this preference, but from a pharmacologic point of view the use of a miotic should be more acceptable.

I am of the opinion that even after the initial period of hyperemia has disappeared atropine would still be indicated if circumcorneal flush and ciliary tenderness should develop, indicating the appearance of iridocyclitis.

Dr. Hugo L. Bair, Rochester, Minn.: I prefer to perform the paracentesis with a keratome, since it provides an opening large enough to permit withdrawal of most of the blood clot and to allow satisfactory irrigation of the anterior chamber with isotonic solution of sodium chloride. It is important to withdraw or wash out as much of the clot from the angle of the anterior chamber as is readily possible without causing trauma to the structures there.

Dr. William B. Clark, New Orleans: A dietary regimen for the relief of intraocular hemorrhage was offered.

To the exclusion of all other foods and liquid, the patient is given every two hours a mixture of 2 ounces (60 cc.) of white Karo corn syrup and 6 ounces (180 cc.) of fruit juice, which may be grapefruit, orange or pineapple. Except for a sedative, which the patient may require, nothing else is administered for a period of more than six days. The author reported rapid clearing of the hyphemia.

Dr. Paul A. Chandler, Boston: I have been accustomed to distinguishing two types of hyphemia. In one, no portion of the iris is visible, and the blood is almost black. In the other, some portion of the iris is visible, and the blood is red. In the first type, in which the blood is black, the surface of the clot is homogeneous. In the second type one can see structure in the clot. In cases in which the anterior chamber is black with blood and the pressure is elevated, I have been accustomed to wash the clot out of the anterior chamber.

In cases in which any portion of the iris is visible and the blood is red, I thoroughly agree with Dr. Rychener that irrigation of the anterior chamber is entirely too radical a procedure. A simple paracentesis can be done if necessary; but in all cases before such a procedure the use of miotics rather than mydriatics is of great importance.

Nonmagnetic Intraocular Foreign Bodies. Dr. Harvey E. Thorpe, Pittsburgh.

Chemically inert intraocular foreign bodies need not be disturbed unless they produce mechanical irritation. They sometimes cause glaucoma.

Differentiation of magnetic from nonmagnetic foreign bodies can be aided by the history of the injury, examination of the tools employed and use of the Berman locator, as well as by examination of fragments from the face or other exposed parts of the body in explosion cases. The use of the magnet for diagnosis is bad practice and should be deprecated.

The presence of multiple intraocular foreign bodies, when they exceed three, suggests conservative therapy for the time being. One must avoid mutilating a globe simply for the sake of removing a foreign body that may be inert. Retinal attachment must be properly and promptly treated. Prompt removal of intraocular foreign bodies is important. The author uses his ophthalmic endoscope for removal of foreign bodies situated deep in the vitreous.

This paper was published in full, with discussion, in the January 27 issue of *The Journal of the American Medical Association*, page 197.

ABSTRACT OF DISCUSSION

Dr. E. B. Spaeth, Philadelphia: The accurate roentgenographic localization of a magnetic foreign body is relatively unimportant as long as one knows (1) the size and the shape of the foreign body, (2) whether the foreign body is intraocular or extraocular and (3) whether it is anterior or posterior to the iris–ciliary body–lens diaphragm. The use of any and all means available for localization—radiopaque markers, scleral rings, contact glasses, iodized oil and injections of air, molded films and filtered roentgen rays—is necessary, though perhaps not in any one individual case.

Major Meyer H. Riwchun, Medical Corps, Army of the United States: In cases in which an intraocular foreign body has been embedded for some time, sulfadiazine therapy may be instituted twenty-four hours prior to operation. Two grams is given at once, followed by 1 Gm. every four hours for two days and then every six hours for two more days, after which its use

may be discontinued unless infection is present. The pars planum approach of Voerhoeff and Fralick is an excellent method of removing magnetic intraocular foreign bodies. It can be used occasionally with nonmagnetic foreign bodies if they are located in this convenient zone, a fine forceps being utilized instead of the magnet. The advantages of this method are absence of hemorrhage, little likelihood of detached retina and practically no danger of sympathetic ophthalmia.

Dacryocystitis: The Transplantation Operation. Dr. Harold Gifford Jr., Omaha.

This article was published in full with discussion, in the December 1944 issue of the Archives, page 485.

Chronic Dacryocystitis: Treatment from the Rhinologist's Point of View. Dr. Laverne B. Spake, Kansas City, Kan.

This article was published in full, with discussion, in the December 1944 issue of the Archives, page 488.

Symposium on Use of Penicillin in Treatment of Diseases of the Eye, Ear, Nose and Throat

Diseases of the Eye. Lieutenant Colonel John E. L. Keyes, Medical Corps, Army of the United States.

Penicillin is the drug of choice in the treatment of ophthalmic diseases secondary to infection with gonococci, streptococci and sensitive staphylococci. The drug should be given a trial in the treatment of diseases caused by Neisseria meningitidis, Neisseria catarrhalis and pneumococci. Its use is optional in the treatment of infections caused by Corynebacterium diphtheriae, Clostridium welchi, Actinomyces bovis and Treponema pallidum.

The relief afforded by penicillin therapy when it is effective is usually prompt, in some instances startling and usually better than that afforded by other modes of medication. Considerable penicillin can be saved by identification of the bacteria present in a disease before treatment is instituted. A primary sensitivity test is recommended in cases of chronic infection caused by staphylococci. An unfavorable early response to the therapy suggests a reappraisal of the case. A virulent, resistant organism may be present.

The use of the substance as a prophylactic with certain intraocular operations and ocular injuries is recommended. Experience suggests that it is better practice to give an overdose than to give an underdose of the drug. Early administration of penicillin in large doses is indicated in cases of orbital cellulitis secondary to infection in the paranasal sinuses and adjacent venous dural sinuses.

Diseases of the Ear. Captain Clifford A. Swanson (MC), U.S.N., and Lieutenant Daniel C. Baker Jr. (MC), U.S.N.R.

Penicillin was found to be of value in the treatment of acute and chronic otitis media, acute mastoiditis and acute labyrinthitis. The drug was employed with success frequently when other forms of therapy had failed. It was possible either to avoid operation for acute mastoiditis or to use the drug with satisfactory results after operation had been performed. When the drug is instilled in the mastoid cavity after operation, healing is prompt and the period of convalescence is shortened.

Diseases of the Nose and Throat. Captain F. J. Putney, Medical Corps, Army of the United States.

Penicillin was used both locally and systemically at Bushnell General Hospital in treatment of some of the more severe and life-endangering infections of the nose and throat. These included orbital complications of disease of the paranasal sinuses, osteomyelitis of the frontal and maxillary bones, epidural abscess, cerebral abscess and thrombosis of the cavernous sinus. Penicillin therapy brought about prompt improvement, and in some cases spectacular results. In general, the acute infections responded more quickly and satisfactorily than the chronic ones.

Abstract of Discussion on Symposium on Penicillin

Major Elmer A. Vorisek, Medical Corps, Army of the United States: My associates and I have used penicillin in a dilution of 500 units per cubic centimeter. In cases of gonococcic ophthalmia the solution was instilled locally, 4 drops every hour, with disappearance of the organisms in conjunctival smears and cultures after twenty-four hours and no recurrences. Intramuscular injections were not given until after the ophthalmic infection was considered cured, except in a case in which the genital gonorrhea was cured with intramuscular injections, this recovery being followed two days later by gonococcic conjunctivitis in the socket of an eye which had previously been enucleated.

Even though negative smears and cultures of conjunctival scrapings may be obtained within twenty-four hours, irrigation with the solution of penicillin should be continued, but at less frequent intervals, until the results of three consecutive daily examinations are reported as negative. We have also used penicillin to irrigate the lacrimal passages in cases of chronic suppurative dacryocystitis, 2 cc. of the 500 unit solution being used daily.

Several patients with orbital cellulitis with proptosis have been seen in consultation with the otolaryngologist, but in each instance penicillin was used intramuscularly, and in 1 case the

abscess also was irrigated with the penicillin. Not only did the cellulitis respond rapidly, but the purulent nasal discharge from all the sinuses promptly cleared up within forty-eight to seventy-two hours.

Major Walter J. Aagesen, Medical Corps, Army of the United States: In our practice my associates and I give 25,000 units of penicillin intramuscularly every three hours day and night for twelve to fourteen days. Especially is this true when the offending organism is the staphylococcus. In cases of chronic mastoiditis, and especially in cases of the acute form with complications, I feel that convalescence is definitely shortened by the use of penicillin. It will not eliminate pus when there is inadequate drainage, and surgical treatment is still of primary importance. We have found the drug effective in treatment of acute otitis media.

Comdr. E. E. Koebbe (MC), U.S.N.R.: My associates and I have treated several hundred patients with early acute otitis media by means of penicillin, and the results have been universally good. We give 15,000 units every three hours around the clock for about seven days, or until the inflammation in the ear drum resolves and the landmarks return. Then we reduce the dose to 10,000 units and maintain that dosage three or four days, after which we give doses of 5,000 units for three or four days longer. We have treated 22 patients with meningitis complicating otitic infection in this way.

We have treated 15 patients with thrombosis of the lateral sinus. In all cases a positive blood culture or occlusion of the lateral sinus or both was demonstrated by operation. Penicillin alone is inadequate in treating thrombosis of the lateral sinus. An operation is necessary, but in no case have we ligated the jugular vein.

Capt. Robert Henner, Medical Corps, Army of the United States: A patient treated with sulfadiazine for about seventy-two hours became moribund and comatose and had a temperature of over 105 F. Institution of intravenous injections of penicillin combined with the intravenous use of a solution of heparin rapidly resulted in a negative blood culture for the Staph. aureus that was previously present, and after a period of recovery of over six weeks he was returned to full duty.

Capt. F. J. Putney, Medical Corps, Army of the United States: I should like to confirm the observation that in cases of thrombosis of the lateral sinus operation must be performed, in addition to treatment with penicillin. My associates and I have treated 8 patients with sinus thrombosis, and in each case the sinus was opened; in a goodly number, however, we were unable to remove the thrombus in the lower end of the sinus, at the jugular bulb, and, also, in these cases we did not ligate the jugular vein.

Capt. C. A. Swanson (MC), U.S.N.: At the National Naval Medical Center, Bethesda, Md., the Penicillin Committee has now allowed penicillin to be used initially in cases of acute otitis media in place of the sulfonamide drugs. This therapy should give even better results. The days before penicillin came into use, it was the experience of my colleagues and myself that mastoid wounds took at least three weeks to heal. We have had only 3 cases in which penicillin was used locally in the mastoid wound, and in all 3 cases healing occurred in eight days.

Book Reviews

Frederick II, Emperor of the Holy Roman Empire. The Art of Falconry, Being the De arte venandi cum avibus. Translated and edited by Casey A. Wood, M.D., and F. Marjorie Fyfe. Price, $10. Pp. 637, with illustrations. Stanford University, Calif.: Stanford University Press; London: Oxford University Press, 1943.

Dr. Casey A. Wood, in searching the mysteries of the organ of vision, sought the solution of the capacity of sight in the eyes of birds. It is well known how patient were his ophthalmic studies of birds at the zoologic gardens and elsewhere, which he described and illustrated in "The Fundus Oculi of Birds, Especially as Viewed by the Ophthalmoscope: A Study in Comparative Anatomy and Physiology" (Chicago, Lakeside Press, 1917). Later, on a sojourn to British Guiana, he gathered heads from the flocks of the many varieties of birds migrated there from the colder countries, which should serve as specimens for later histologic study. His interest in avian subjects, however, led him to the realization that to comprehend them he, necessarily, should become more or less seriously an ornithologist. Yet, in that new study he always maintained that his primary object was to learn more and more about the mysteries of sight. Quite naturally, he eagerly sought most from the nature of birds of prey and rapacious birds, hoping to discover the source of the marvelous power which enables them to detect their quarries at long, long distances, remote from the point of their rising into the air. The habits of buzzards, eagles, hawks and other rapacious birds are well known to every one who has spent much time in the wilds. One is led to wonder: Is it sight or smell that incites one of a flock of buzzards sailing in circles high up in the air suddenly to dart down into the plain and seize a rabbit or squirrel which had moved out from the thicket?

(This reviewer recalls, while on the voyage from the ophthalmologic congress held at Amsterdam, the extraordinary flights of a pair of English sparrow hawks which had lived for several weeks on the ship, roosting in the shrouds stretched from the foremast. While apparently simply resting, though the seas were rough and black from the skies being overcast, they would suddenly dart over the ocean to alight at a far distant trough and then return as swiftly as they had left, carrying a small petrel struggling in their talons, which they proceeded to devour while clinging to the ropes. Thus they manifested, in the midst of conflicting lights and shadows, visual acuteness beyond the human observer's acquiring.)

Through this aspect of his investigations, Dr. Wood became deeply interested in the medieval practice of "Hawking," an interest which led him to delve into the life history of that prince of hawkers, King Frederick II, of Hohenstaufen (1194-1250). To that history Dr. Wood devoted the last years of his life, with the highly efficient assistance of his niece, Miss Fyfe, preparing for publication a monumental and beautiful volume on "Falconry," in translation of Frederick's "De arte venandi cum avibus," from manuscripts prepared by the king up to the middle of the thirteenth century.

King Frederick should be of interest to the medical profession, as he did much to advance medical education and to regulate practice. By his edicts, there were required three years in premedical studies, a five year course of medical study, followed by a year of practical work, and, in order to receive the license, an examination by the state.

This work should be of interest to ophthalmologists, although it is not an ophthalmologic treatise, because it describes minutely the practice of hawking and the several varieties of hawks and because the whole success of that practice depends on the visual powers of another order of animal. A brief chapter on the eyes of the birds describes simply the gross appearance of the organ in the varieties employed.

The book is both a contribution to the history of science and an account of a distinct element in medieval culture. In itself, the volume is surpassingly beautiful, containing 186 plates, which can serve as an iconography of falconry. And it stands as a monument to American scholarship and the art of the printing and making of books.

BURTON CHANCE.

Doctors at War. Edited by Morris Fishbein, M.D., with 15 other contributors. Price, $5. Pp. 418, with 82 photographs, charts and diagrams. New York: E. P. Dutton & Co., Inc., 1945.

In World War I 8.1 per cent of the wounded died; in World War II it was only 3.3 per cent. In the former conflict the death rate from disease was 15.6 per thousand; in the latter, only 0.6. This book tells how the reduction was accomplished. The Surgeons General of the Army and Navy describe the work of their departments in general. Surgery is discussed by Brig. Gen. F. W. Rankin; air medicine, by Maj. Gen. D. N. W. Grant, and convalescence and rehabilitation,

by Col. H. A. Rusk. Maj. Gen. P. R. Hawley, describes medical preparation for D-Day, and Capt. F. R. Moore recalls his medical activities on Guadalcanal and Tarawa. On the civilian side, Surgeon General Parran describes the Public Health Service in wartime; Dr. C. W. Griffiths writes of the Veterans Administration; Dr. G. Canby Robinson discusses the American Red Cross; Dr. G. B. Darling, the National Research Council, and Dr. H. S. Diehl, the doctor's work at home. Allocation of medical services is taken up by Maj. Gen. George F. Lull, and selective service is discussed by Col. L. G. Rowntree.

The magnitude of the medical tasks undertaken by the armed forces can hardly be grasped by a layman. He will be impressed by figures and statistics, but he will only sense the sacrifices of life, health and prospects implied in every line of this text.

The medical officer may well be proud of himself and his record, but he should enjoy his feeling of self respect while he can. The poor devil has worries enough, but it may be salutary for him to read a significant interpretation of his effort and sacrifice:

"It is interesting to note," writes a reviewer of this book in the *New York Herald Tribune* of May 13, 1945, "how much can be done by doctors . . . where there are no private patients, no fees, and no patient has the right to choose his doctor." The politicians are already preparing the welcome and the reward for the "doctor at war."

COMDR. G. M. BRUCE.

Neuro-Ophthalmology. By Donald J. Lyle, B.S., M.D., F.A.C.S. Price $10.50. Pp. 398, with 7 charts and 529 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1945.

Dr. Lyle has presented a seemingly complex subject in such an interesting way that all ophthalmologists should be stimulated to start and/or continue the application of neurology to ophthalmology, inasmuch as the two are inseparable.

This book is profusely illustrated with original charts, fundal photographs, roentgenograms and visual field charts to correlate the anatomic, neurologic and ophthalmologic changes produced by developmental, inflammatory, vascular, neoplastic and traumatic lesions affecting the central nervous system. The extensive bibliography is more than sufficient to stimulate collateral reading.

Although the common and rare ocular syndromes are described, the ophthalmologic portion usually is quite overshadowed by a too detailed anatomic and neurologic description. But, all in all, Dr. Lyle's book is a much needed addition to every library and is highly recommended. The author is to be congratulated for a job well done.

W. I. LILLIE.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

Faculty of Ophthalmologists

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2., England.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. N. McAlister Gregg, 193 Macquarie St., Sydney.
Secretary: Dr. D. A. Williams, 27 Commonwealth St., Sydney.
Place: Sydney:. Time: Oct. 3-6, 1945.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secetary, Dr. Mohammed Khalil.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Silvio de Almeida Toledo, Barão de Ilapetininga St., 88, 5º Andar, São Paulo, Brazil.
Secretary: Dr. Plinio de Toledo Piza, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

Sociedade de Ophthalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4, III tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

American Ophthalmological Society

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

Association for Research in Ophthalmology, Inc.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

Canadian Medical Association, Section on Ophthalmology

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Theodore L. Terry, 140 Marlborough St., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. James H. Mathews, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE and THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnstown, Pa.
Secretary-Treasurer: Dr. J. McClure, Tyson, Deposit Nat'l Bank Bldg., Dubois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Medical Society of the State of Pennsylvania, Section on Eye, Ear, Nose and Throat Diseases

Chairman: Dr. Karl M. Houser, 2035 Delancey St., Philadelphia 3.
Secretary: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Edmond L. Cooper, 1553 Woodward Ave., Detroit 26.
Secretary: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. E. B. Fairbanks, 315 Medical Arts Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Dean Spear, 516 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn 11.
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. William H. Howard, 389 Linwood Ave., Buffalo 9.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo 9.
Time: Second Thursday of each month from October to May.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Samuel J. Meyer, 58 E. Washington St., Chicago 2.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.
Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.
Secretary: Dr. H. H. Wygand, Guardian Bldg., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.
Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.
Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Dr. William S. Summers, 1613 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur S. Hale, 1609 Eaton Tower, Detroit.
Place: Club rooms of Wayne County Medical Society.
Time: First Wednesday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmoological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Francis Carl Hertzog, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Robert G. Thornburgh, 117 E. 8th St., Long Beach, Calif.
Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Secretary-Treasurer: Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montreal Ophthalmological Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6.30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: James Robertson Hotel. Time 6:30 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Rudolf Aebli, 30 E. 40th St., New York.
Secretary: Dr. Truman L. Boyes, 654 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Maurice L. Wieselthier, 1322 Union St., Brooklyn.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. A. A. Steinberg, 1502 Farnam St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha 2.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351-5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Isaac B. High, 326 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. Vincent Jones, 634 N. Grand Blvd., St. Louis.
Secretary: Dr. T. E. Sanders, 508 N. Grand Blvd., St. Louis 3.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey, 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. L. C. Ravin, 316 Michigan St., Toledo 2, Ohio.
Secretary: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.